THE Review of Gastroenterology

VOL. 20, NO. 5 MAY, 1953

SYMPOSIUM ON BLEEDING ESOPHAGEAL VARICES AND THE PROBLEM OF PORTAL HYPERTENSION

Portal Systemic Shunts in the Management of Portal Hypertension with Massive Gastrointestinal Hemorrhage

A Clinical Evaluation of Ligation of the Hepatic and Splenic Arteries in Treatment of Cirrhosis of the Liver

Physiology and Pathology of the Cirrhotic Liver

Mediastinal Packing for Bleeding Esophageal Varices Associated with Portal Hypertension

Eighteenth Annual Convention
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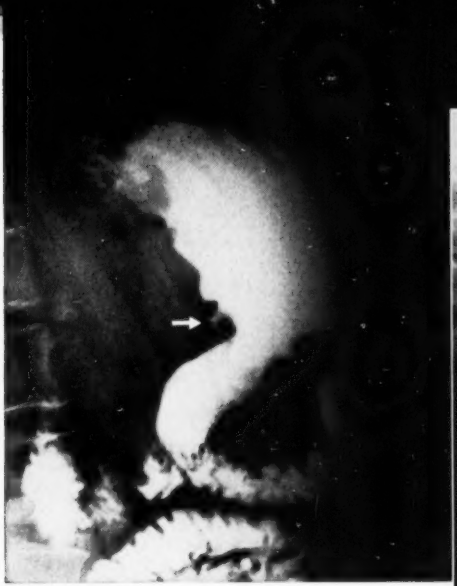
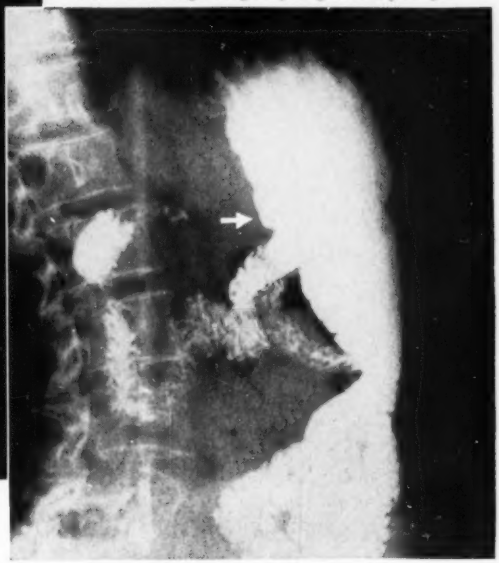


Fig. 1: "Roentgen examination . . . revealed the ulcer to be very much in evidence."

Fig. 2: In ten weeks "the ulcer niche was no longer in evidence roentgenologically or gastroscopically."



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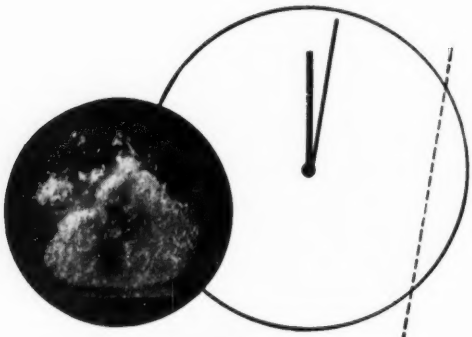

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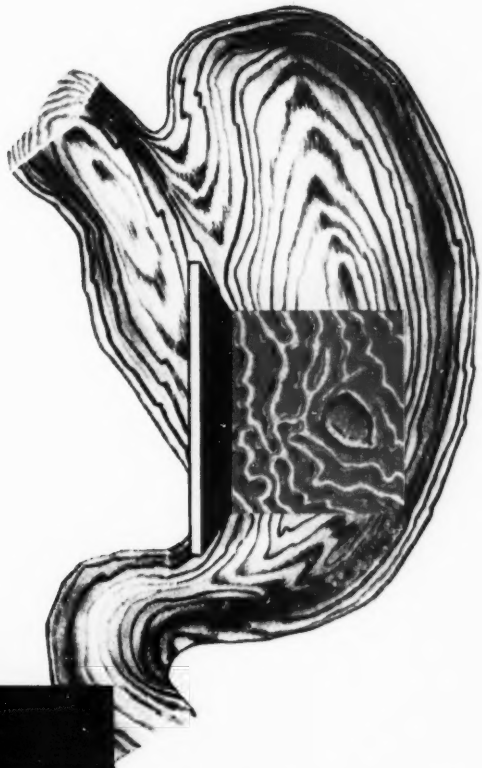

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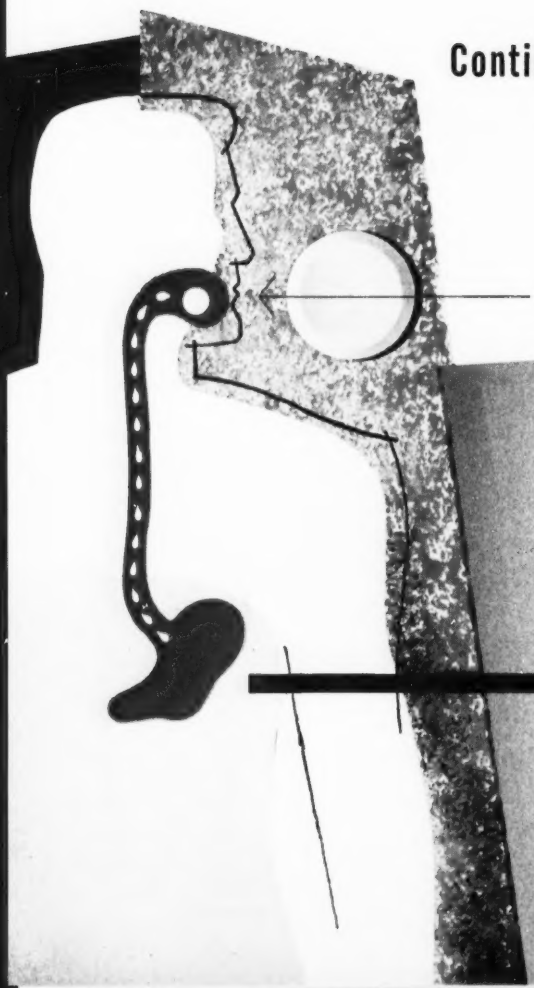

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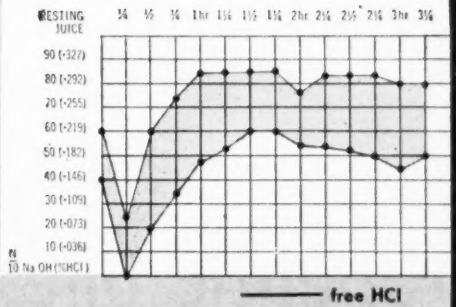
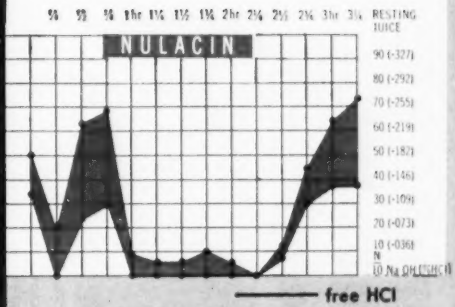
1. Douthwaite, A. H., and Shaw, A. B.: The Control of Gastric Acidity, Brit. M. J. 2:180 (July 26) 1952.
2. Douthwaite, A. H.: Medical Treatment of Peptic Ulcer, M. Press 227: 195 (Feb. 27) 1952.



GASTRIC ANALYSIS. Superimposed gruel fractional test-meal curves of five patients with peptic ulcer.



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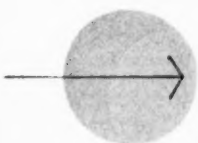

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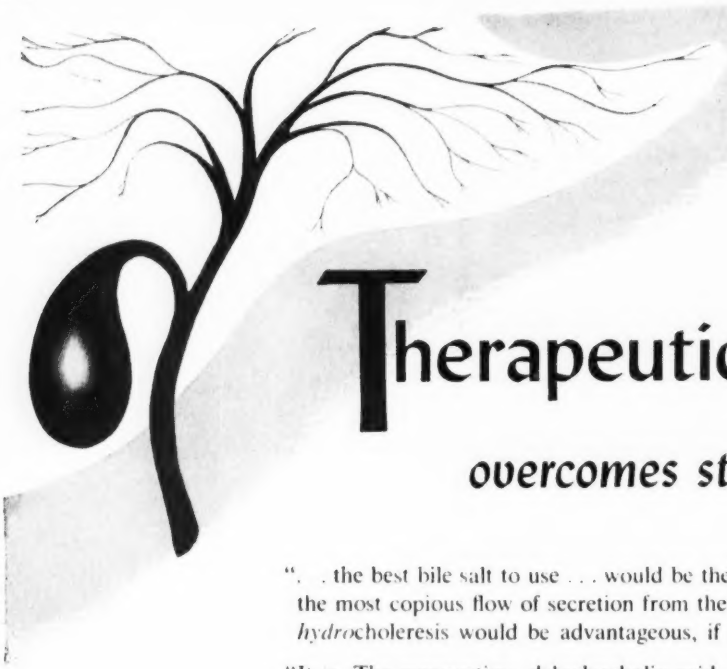

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*Beckman, H.: Pharmacology in Clinical Practice, Philadelphia, W. B. Saunders Company, 1952, p. 361.

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THE Review of Gastroenterology

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(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

VOLUME 20 MAY, 1953 NUMBER 5

SYMPOSIUM ON BLEEDING ESOPHAGEAL VARICES AND THE PROBLEM OF PORTAL HYPERTENSION*

SAMUEL HARBISON, M.D.†

Pittsburgh, Pa.

This subject today of bleeding esophageal varices is an exceedingly complex and serious one. We all realize that once a cirrhotic patient bleeds, or once a patient with a block in the portal system bleeds, his life expectancy is markedly shortened. We are interested primarily in treating the patient for a symptom in order to prolong his life.

The symposium today takes in many of the procedures which have been used up to the present time, surgical procedures, in an effort to treat esophageal hemorrhage. Perhaps only one or two of the suggested operations for cirrhosis of the liver have any direct connection with the treatment of the cirrhotic state or the treatment of the underlying diseases.

The whole subject brings up many interesting facets from the standpoint of physiology, whether or not we are on the right track. I should like to have some of the eminent speakers bring out one of the most fundamental problems, whether or not high blood pressure in the portal system has anything to do with actual formation of esophageal varices, even though we know that the procedure of shunting and lowering the portal hypertension is perhaps the most effective procedure we have today.

If you think Dr. Lord's presentation on the shunting of veins, the creation of an internal fistula, is a rather remarkable procedure for this symptom, then consider the next paper, which has to do with the totally outrageous physiological concept of ligating the hepatic artery in an attempt to help the disease of the liver. I am sure that Dr. Madden has seen an amazing incongruity in this procedure. I myself have carried it out on a few occasions and I am very anxious to hear his paper on the subject.

*Presented before the Seventeenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 20, 21, 22 October 1952.

†Moderator.

I hope these first two presentations will present the problem which some doctors, most of whom are internists, have foisted upon us as surgeons because of the seriousness of the symptom of bleeding.

The latter part of this symposium will go a little more deeply into the physiology of the liver and will include a discussion of a further method of trying to control the problem by increasing the number of portal systemic anastomoses by mediastinal packing.

We will hear a little more of the answer to this very interesting problem from the standpoint of the underlying physiology and pathology of the cirrhotic liver.

PORTAL SYSTEMIC SHUNTS IN THE MANAGEMENT OF PORTAL HYPERTENSION WITH MASSIVE GASTROINTESTINAL HEMORRHAGE*

JERE W. LORD, JR., M.D.

New York, N. Y.

The most serious complication of portal hypertension is massive gastrointestinal hemorrhage from esophageal and gastric varices. The mortality rate has been estimated[1,2] to be approximately 25 per cent with the first hemorrhage and 50 per cent in the survivors with the second hemorrhage when the underlying cause is an intrahepatic block, i.e. some form of cirrhosis of the liver. In Shull's[3] series, five out of seven patients, or 71 per cent, died from hemorrhage in the group of patients with extrahepatic block of the portal bed. There is little need to labor the point that massive gastrointestinal hemorrhage is of the most serious import when proven to be on the basis of portal hypertension.

The diagnosis usually can be made by a careful history, the physical examination, an esophagram and an analysis of a selective group of liver function tests. The differential diagnosis of the intrahepatic from the extrahepatic type of portal hypertension rests in the final analysis on the presence or absence of impaired liver function. We have obtained valuable information from the following tests: serum albumin, prothrombin time, cephalin flocculation, serum bilirubin, cholesterol and cholesterol esters, and the bromsulfalein excretion test. In the typical case of extrahepatic portal bed block, the above tests are normal whereas in those patients with an intrahepatic block, all are to a greater or lesser degree abnormal.

Therapeutically, the patients with an extrahepatic portal block are best managed by splenectomy with an associated splenorenal shunt when indicated. The decision to rely only on a splenectomy is made during the operation based on careful measurements of the pressures in the various parts of the portal tree. Occasionally the block is located in the splenic vein peripheral to the entrance of the coronary vein and splenectomy alone will suffice by eliminating the engorged venous connections between the spleen and the stomach. Even more rare is the patient whose splenic hypertension is due to an arteriovenous fistula or aneurysm of the splenic artery and again splenectomy with removal of the aneurysm or arteriovenous fistula will result in cure. In all other cases of an extrahepatic block a splenorenal shunt is indicated, usually by an end-to-side suture anastomosis. One may use an autogenous vein graft from the femoral vein as recommended by Rousselot[4] in order to eliminate the necessity of dissecting a long segment of the splenic vein. Many of the patients have a well-

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*Read before the Seventeenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 20, 21, 22 October 1952.

From the Department of Surgery, New York University Post-Graduate Medical School and the Fourth Division, Bellevue and University Hospitals.

developed secondary hypersplenism and a salutory effect is noted on the peripheral blood elements following splenectomy and a splenorenal shunt. All surgeons interested in this field employ the combined thoracoabdominal incision either through the 9th or 10th interspaces or with resection of the anterior half of the 10th rib. The operative mortality rate has been in the neighborhood of five per cent and the postoperative incidence of hemorrhage has been extremely low. When it occurs, the usual explanation has been thrombosis of the anastomosis.

Less unanimity of opinion holds for the type of shunt best suited for the patient with an intrahepatic block. In the first place, no surgeon has been rewarded with a successful outcome in the patient with cirrhosis, portal hypertension and massive hemorrhage when the portacaval shunt was performed as an emergency. Although the well-prepared cirrhotic liver will tolerate great operative insult, the unprepared organ will invariably go into irreversible failure following an operative procedure of magnitude. Therefore, it is necessary for the ultimate survival of the patient to control hemorrhage, restore a measure of hepatic functional reserve and then carry out one or another type of portal systemic shunt. The balloon tamponage as advocated by Blakemore[5] as well as many others has worked well in the hands of most surgeons. Hemorrhage is controlled, gastric feedings of a high protein and high vitamin content begun, and the patient transfused to raise the hematocrit to 40 per cent. Intravenous glucose with vitamins supplement fluid requirements to the total of 4,000 to 5,000 c.c. per day. It has long been known, and is also probably sound, that the cirrhotic liver functions better when there is a large fluid intake rather than a severely limited one, i.e. 1,500 to 2,000 c.c. per day. In many patients the balloon can be removed in two to three days and oral feedings of soft consistency administered. Crude liver extract injected intramuscularly daily is probably of value. In general, five to nine days of this type of therapeutic regimen will bring the patient to operation in excellent condition. If one waits more than seven to nine days there frequently ensues another massive hemorrhage from which greater difficulty may be encountered in improving hepatic function. During the week of preparation, if the slightest sign of bleeding is noted, the balloon is replaced and left *in situ* and the patient taken to the operating room after the five to nine day period of preoperative therapy.

Recently Linton[6] has recommended a direct attack on the bleeding varix by a transthoracic approach and then when the patient is well prepared for a portacaval shunt to do so after an interval of two to six weeks. The author has had no personal experience with the above procedure.

The choice between an anastomosis of the portal vein to the inferior vena cava on the one hand and a splenorenal anastomosis on the other seems to rest entirely on the surgeon's personal experience with the two operations. Rousselot and Linton favor the splenorenal anastomosis, the former exclusively and the latter as a general rule. Blakemore favors the portal-vena caval anastomosis

generally and Johnston also uses it by preference. For my part, I have found the portacaval anastomosis less difficult and less tedious, more constant in the size and strength of the structures and more frequently patent when studied at the autopsy table when death has ensued either early or late following the operative procedures. Although many other surgeons have avoided serious technical problems during the dissection of the veins necessary for the anastomosis, it has been the author's experience to encounter difficulty several times during his earlier experience with each type of shunt and although the mistake may seem relatively small in this group of patients, the margin of safety is also very small. Whereas we have employed the right thoracoabdominal approach[7,8] to portacaval anastomosis for several years, an unfortunate experience coupled with Johnston's paper[9] led us to employ, during the past six months, a long right paracostal incision from the midline to the posterior axillary line with the patient's right side elevated 30 degrees. Excellent exposure has been obtained and we eliminated the postoperative chest complication which led to a postoperative death in an otherwise perfectly executed shunt. A 51 year old white cirrhotic woman with satisfactory liver function was subjected to a portacaval shunt through a right thoracoabdominal approach with resection of the anterior two-thirds of the ninth rib for repeated episodes of gross and massive gastrointestinal hemorrhages. Slow intrapleural oozing of blood occurred postoperatively and was not controlled by repeated thoracentesis. Thoracotomy was performed 48 hours postoperatively and a bleeding point in the intercostal muscle was controlled. In spite of repeated blood transfusion and supportive therapy death ensued two days later from hepatic failure. Autopsy revealed an excellently constructed and functioning portacaval shunt.

Blakemore has shown that it is possible to carry out portal systemic shunts in patients with cirrhosis of the liver with an operative mortality of nine per cent in the group with good liver function and 45 per cent in the group with poor liver function, with an overall mortality of 21 per cent. This is in contrast to the mortality from medical management alone of approximately 70 per cent within two years in the same type of patients who have had one or more major gastrointestinal hemorrhages.

In the most recent 11 patients subjected to an end-to-side portacaval shunt there have been three deaths. One was cited above; the second patient suffered from severe posthepatitic cirrhosis of several years' duration. There was evidence of obstruction of the intrahepatic bile ducts with a high alkaline phosphatase (15.5) and marked jaundice. The serum albumin was 3.8 gm. per cent and repeated massive gastrointestinal bleeding interfered with optimal hepatic preparation. Death occurred from hepatorenal failure 12 days postoperatively. Autopsy showed a well-constructed and functioning end-to-side portacaval shunt. The third death took place in a 48 year old white man with repeated massive gastrointestinal hemorrhages, the one leading to surgical interference being controlled only by continuous use of balloon tamponage for five days prior to operation.

An end-to-side portacaval shunt was constructed with difficulty due to the wide gap between the portal vein and the inferior vena cava. Postoperative hemorrhage led to death on the fifth day. Permission for autopsy was not granted but it was thought that the anastomosis had most likely thrombosed.

Of the remaining eight patients, one died three months following portacaval shunt performed for repeated massive hemorrhage from acute yellow atrophy secondary to homologous serum jaundice engrafted on a posthepatitic cirrhosis. She had been in excellent health, free from hemorrhage for two and one-half months. Six blood transfusions were required preoperatively to compensate for the massive hemorrhage leading to the shunting procedure and four more were given during the operation. One of the 10 pints of blood apparently carried the virus. From the time of her first symptoms of anorexia, fever and icterus, death occurred in eight days in spite of the intensive supportive measures. Autopsy confirmed the diagnosis of acute yellow atrophy engrafted on a posthepatitic cirrhosis and also demonstrated an excellently constructed functioning anastomosis.

Of the remaining seven patients, all but one have been in excellent condition, free from gastrointestinal bleeding. The one patient in question had a massive hemorrhage four weeks following an apparently successful portacaval shunt and required a high subtotal gastric resection. He has remained well since the second operation four months ago.

Summary

The most important and serious complication of portal hypertension is massive gastrointestinal hemorrhage. The mortality rate is approximately 25 per cent for the first hemorrhage and 70 per cent of the patients are dead within two years of their first hemorrhage when conservative measures are employed. To date, portacaval shunts are the most effective way to control hemorrhage due to portal hypertension. The operative mortality rate is approximately 45 per cent in patients with poor liver function and 10 per cent in those with good hepatic function. In the group of patients with extrahepatic block (normal liver function), a splenectomy and splenorenal shunt is followed by an excellent result in the vast majority of patients with an operative mortality of approximately five per cent.

The choice of procedure in patients with intrahepatic portal hypertension usually is related to the surgeon's personal experience with various types of shunts. The author favors an end-to-side portacaval anastomosis as the most satisfactory operation. Shunting operations are not simple or easy and each surgeon has to overcome the technical problems with experience and careful selection of patients. Most surgeons hesitate to reject a patient as a poor risk but those who do unquestionably will be able to report more favorable mortality figures.

With few exceptions, those patients who leave the hospital alive remain well and free from hemorrhage. With technical proficiency and careful and thorough pre- and postoperative care, the overall salvage rate of patients with intrahepatic portal hypertension will approach 85 per cent and in the group of extrahepatic portal block will approach 95 per cent.

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A CLINICAL EVALUATION OF LIGATION OF THE HEPATIC AND SPLENIC ARTERIES IN THE TREATMENT OF CIRRHOSIS OF THE LIVER*

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In April, 1951, Rienhoff reported satisfactory results in the treatment of cirrhosis of the liver with associated hematemesis and ascites by ligation of the hepatic and splenic arteries. The hepatic artery was ligated distal to the gastroduodenal artery.

During a period of 13 months from June, 1951, to July, 1952, eight patients with cirrhosis of the liver complicated by ascites and/or hemorrhage were operated upon. In six a combined ligation of the hepatic and splenic arteries was done and in two the hepatic artery only was ligated. The ligature on the hepatic artery was distal to its gastroduodenal branch in one patient and proximal to the gastroduodenal artery in the remaining seven patients. Of the eight patients, six were men and two were women. In two patients hematemesis was present. In one it was the primary and only symptom and in the other it was associated with ascites. In the remaining six patients chronic recurrent and intractable ascites was the primary indication for operation. In five of the eight patients a direct recording of the portal venous pressures in millimeters of saline was obtained by the insertion of a No. 18 gauge needle into the lumen of the portal vein. In all a portal hypertension was present. The highest was 482 and the lowest was 321 millimeters of saline. The portal venous pressure was again recorded after ligation of the hepatic (proximal to the gastroduodenal artery) and splenic arteries respectively. In two instances the fall after ligation of the hepatic artery exceeded that which occurred after ligation of the splenic. In two others the reverse was true. In the remaining patient the hepatic artery alone was ligated and accordingly a comparative study was not possible. The maximum fall in the portal venous pressure after the combined ligation of the hepatic and splenic arteries was 61 millimeters of saline and the minimum was 20 millimeters of saline.

Of the eight patients operated upon, four (50 per cent) died. In one patient cardiac arrest occurred while the closure of the skin was being completed. Direct manual massage of the heart was unsuccessful. Necropsy showed an acute coronary thrombosis. Another died of massive and uncontrollable intraperitoneal hemorrhage. Hemorrhage suddenly occurred during the course of the operation and was characterized by a "weeping" from the surface of all of the exposed tissues. The wound was packed but hemorrhage recurred three hours postoperatively

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and the patient expired. In a third patient operation was performed in a desperate attempt to control acute and recurrent exsanguinating hematemesis from bleeding esophageal varices. Forty hours postoperatively, however, a sudden massive hematemesis occurred and the patient died. The fourth patient died nine days postoperatively. The cause of death was renal insufficiency. Oliguria occurred on the fifth postoperative day, followed by complete anuria and death on the ninth postoperative day. A necropsy showed cloudy swelling of the kidneys. There was no evidence of necrosis of the liver or the spleen.

The follow-up period in the remaining four patients is 15 months, 7 months, 4 months, and 3 weeks respectively. The first patient operated upon continued to imbibe freely of alcohol and did not maintain an adequate diet. Seven months after operation the patient was admitted to the hospital in extremis and death within three hours occurred. Necropsy showed ruptured esophageal varices and a partial recannulization of the lumen of the ligated hepatic artery. Necrosis of either the liver or the spleen was not present. The second patient was readmitted to the hospital eight months postoperatively because of oropharyngeal bleeding and recurrent ascites. At the present time, 15 months postoperatively, the condition of the patient is considered poor. This is the only living patient. In the third patient, operated upon for persistent ascites, hematemesis occurred for the first time three weeks postoperatively. Within 20 hours hepatic insufficiency, coma, and death occurred. At necropsy there was no necrosis of the liver or the spleen. The fourth patient died four months postoperatively. The indication for operation was intractable ascites. During the first two months postoperatively, improvement in the general condition of the patient was marked. During the succeeding two months, however, repeated abdominal paracenteses were required because of recurrent ascites. At the time of the last paracentesis transgression of the lumen of the intestine occurred with a complicating peritonitis which was the immediate cause of death.

The efficacy of ligation of the hepatic and splenic arteries in the treatment of cirrhosis of the liver complicated by ascites, hemorrhage, or both, is seriously questioned. From a study of the results obtained its continued use is not recommended.

PHYSIOLOGY AND PATHOLOGY OF THE CIRRHOTIC LIVER*

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In keeping with the general theme of the symposium, we will limit this discussion to a consideration of only those aspects of the physiology and pathology of cirrhosis which are directly concerned with the problem of portal hypertension. Increased portal pressure is frequently encountered as a complication of advanced cirrhosis, but is by no means limited to this condition. Thrombosis of the portal or splenic vein, an inflammatory lesion of the portal bed, a tumor or a congenital venous anomaly may impede the flow of portal blood and offer a plausible explanation for the development of increased venous pressure. This has been designated by Whipple as an *extrahepatic* obstruction to portal blood flow. When portal hypertension develops in patients with cirrhosis, however, no obvious obstruction to portal blood flow within the portal vein or its tributaries can be demonstrated. Therefore, if such an obstruction exists it must be within the liver itself, i.e. an *intrahepatic block.*

This concept of an increased head of portal pressure secondary to an obstruction of the portal outflow tract is an attractive hypothesis, deceptively simple.

If this were a straightforward obstructive phenomenon, it should be possible to reproduce the condition by partial or complete occlusion of the portal vein or its tributaries. Child attempted to do this. He occluded the portal vein both in the monkey and in man and produced the expected rise in portal pressure. This increase, however, was not maintained and the portal pressures consistently returned to a normal level in 1-2 weeks, coinciding with the development of collateral circulation. These collaterals were in no sense more extensive than those commonly seen in cirrhosis of the liver where high portal pressures are maintained throughout the course of the illness. Thus, we see that even in the case of a straightforward extrahepatic obstruction, the problem of maintenance of the portal pressure has not been solved, and the exact role played by the obstruction is not known. In considering the role of cirrhosis in the production and maintenance of high portal pressure, even more difficulties are encountered. It would seem worthwhile, therefore, to re-examine critically the pathology and physiology of the cirrhotic liver to determine: (1) to what extent portal vein blood is actually impeded in its flow through the liver and (2) to consider other factors in cirrhosis besides obstruction which might influence the pressure relationships in the portal vein.

One of the most prominent features of the cirrhotic liver is fibrosis. This appeared to the older pathologists to start in the portal areas and to spread gradually in broad connective tissue bands around the lobule isolating the par-

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enchymal liver cells from their blood supply. From these observations arose the term "portal cirrhosis". From this basic concept of the pathological anatomy of the liver, it would be logical to deduce that the fibrous tissue mass in the portal area choked off the entering blood supply from both the portal vein and hepatic artery and produced a distal congestion or hypertension.

In 1947 Ashburn cast serious doubt on the portal origin of the connective tissue masses. He showed in experimental cirrhosis, both dietary and carbon-tetrachloride induced cirrhosis of rats and guinea pigs, that the septal vessels could only be injected by way of the hepatic vein, and could not be reached from the portal vein side. This would indicate that the blood supply of the septum was intimately connected with the hepatic and not with the portal vein. It would also follow that the septum was not portal in origin, but started at the center of the lobule, adjacent to the central hepatic vein and spread secondarily to the portal areas. In experimental choline deficiency cirrhosis of rats, Hartroft, working in Best's laboratory, showed the same sequence of events could be demonstrated with fat stains. When animals were sacrificed serially, early in the course of their disease fat cysts, centrally located, could be easily outlined. These coalesced into larger and larger droplets and were replaced by scar tissue around the central vein. If the animals were followed long enough, these connective tissue masses eventually involved the portal area as well.

In man this is more difficult to demonstrate since autopsy specimens usually represent advanced stages of cirrhosis. Recently, Popper, Elias, and Pelty attempted to work out these relationships using 12 human autopsy specimens of livers with cirrhosis. The hepatic vein, portal vein, and the hepatic artery were injected with different colored media. The septal vessels outlined in these preparations showed filling from both the hepatic and the portal bed, that is, portocentral origin instead of purely central origin. This resembles the late stages of the experimental preparations which also became portocentral if the liver damage was allowed to progress for a sufficiently long time. The results are not conclusive, but are consistent with the animal experiments.

The dynamic concept of centrilobular necrosis advanced by Himsworth lends credence to the theory of central fibrosis advanced by the experimental pathologists. At intervals, after administration of carbon-tetrachloride subcutaneously in rats, Himsworth injected India ink into the spleen. In normal animals the intralobular sinusoids, the portal vessels, and the hepatic veins filled readily. Two hours after carbon-tetrachloride injection, however, before necrosis had time to appear, the ink was excluded from the central zone of the lobules while it filled the peripheral parts of the intralobular sinusoids. This was a dramatic demonstration that small doses of a toxic agent could cause swelling of the parenchymal cells, and this peripheral swelling in turn obstruct the flow of blood through the sinusoids. By the time the blood reached the center of the lobule, it had been depleted of substances necessary for the life of the cell, and necrosis

of these cells resulted. The necrosis and resulting fibrosis occurred not at the port of entry, the portal area, but in the center of the lobule, the site of ischemia. This is the picture in the majority of common diseases of the liver. It is seen after poisoning with various toxic agents; it is the typical lesion in infectious hepatitis and homologous serum jaundice.

If this experimental work can be substantiated in human cirrhosis, and the origin of the fibrosis established as central rather than portal, it will revise the current concept of portal fibrosis and its significance in the production of portal hypertension.

In a consideration of possible causes of obstruction within the liver, which could bear on the problem of portal hypertension, attention should be called to the suggestion of Kelty, Baggenstoss, and Butt that regenerating liver nodules impinge upon the vascular bed causing obstruction. These workers made careful scaled wax reconstructions of the cirrhotic liver and demonstrated large nodular masses compressing and actually obstructing the venous channels. This may partially explain the flattening and compression of the vascular twigs surrounding the nodules of parenchymal tissue, and may also offer an explanation for the progressive nature of the cirrhotic process. These interesting concepts of intrahepatic obstruction are backed up by much experimental evidence, but it is yet to be shown to everyone's satisfation that the problem of portal hypertension in cirrhosis is actually one of obstruction to portal blood flow.

Another aspect of the problem of portal hypertension assuming increasing importance is the intrahepatic circulation. You are familiar with the work of Herrick, who profused normal human and cirrhotic livers, obtained at autopsy, to study the relationship of portal vein pressure to hepatic artery pressure. In profusing normal livers, when the portal pressure was maintained at 10 millimeters of water, an increase of 40 millimeters in arterial pressure was necessary in order to effect a rise of one millimeter in portal vein pressure. In cirrhotic liver, however, a comparable rise of one millimeter of portal pressure resulted from every six millimeters rise in arterial pressure. Herrick, threfore, concluded that in the cirrhotic liver there existed a freer communication between the arterial and portal circulation. He also believed that there was increased arterial supply to the cirrhotic liver. In profusing normal livers with portal pressure maintained between 10 and 20 millimeters of water, portal flow always appreciably exceeded arterial flow. This was not a new observation, for it was well known that normally the portal veins supply more blood to the liver than does the hepatic artery. In profusing cirrhotic livers, however, it was necessary to raise portal pressure above 40 millimeters of water in order to render portal flow greater than arterial. Thus, Herrick reasoned that portal flow was less than arterial flow in the cirrhotic liver, except in far advanced cirrhosis, where the elevated portal pressure kept normal or nearly normal amounts of blood flowing through the liver. He attributed the increase in portal pressure to two factors: (1) more direct communication between the arterial tree and the portal vein, (2) increased volume of blood sup-

plied to the liver by the hepatic artery. He believed that both of these factors operated to transmit arterial pressure more freely to the venous side.

McIndoe, using the same technic, was unable to duplicate these observations of Herrick. He pointed out the marked diminution of the total vascular bed and was unable to find any evidence of sinusoids between the portal and hepatic venous trees.

Dock, in 1942, attempted to repeat these experiments of Herrick and McIndoe. He obtained different results in his alcoholic and nonalcoholic cirrhotic livers, showing an increase in arterial profusability in the alcoholic cirrhotics. This, he was not able to demonstrate in the nonalcoholic cirrhotics. As a result of his studies, he postulated a reciprocal relationship between the hepatic artery and the portal venous flow, proportional to the degree of both arterial pressure and intrahepatic resistance.

While tracing the development of the fibrous tissue in the septa, in the preparations discussed earlier in this paper, Popper and his co-workers were able to demonstrate multiple portahepatic anastomoses in the cirrhotic liver. Very few anastomoses could be demonstrated between branches of the portal vein, more between branches of the portal vein and hepatic artery and many between branches of the portal and hepatic veins. These, he felt, developed from pre-existing sinusoids and constituted multiple internal Eck fistulae shunting the blood directly from the portal to the hepatic veins. It was suggested that the development of these portahepatic vascular anastomoses presents the irreparable stage in cirrhosis, maintaining the process after the etiological factor has disappeared.

While communications from a high pressure hepatic arterial system to a lower pressure venous portal system may well affect the pressure relationships of the portal vein, it is difficult to interpret the portal vein—hepatic vein, venovenous shunts. As the authors point out, these small shunts direct blood away from the parenchymal cells and lead to progressive cellular damage. Theoretically, however, they should not cause an elevation of pressure in the portal vein, but should tend to relieve any hypertension that has previously developed.

At the present time, our concepts of both the pathology and physiology of the cirrhotic liver are changing rapidly, due to the enormous amount of experimental work on the liver now in progress. Portal hypertension, in turn, will probably be shown to be related to a combination of many interrelated factors, rather than the result of any one set of circumstances.

Discussion

Dr. Samuel Harbison (Pittsburgh, Pa.):—The problem is by no means solved at the present time as you can see. It is interesting that clinical observation

supports these experimental findings of Herrick, in that most men who have gone in to ligate the hepatic artery for portal hypertension, bleeding, or ascites, or all of them, have noticed the large size of the hepatic artery, which is a condition known to exist proximal to an arteriovenous fistula.

There has been a more recent attempt which will be described by Dr. Kent, having to do with the packing of the mediastinum in the area of the esophageal varices.

MEDIASTINAL PACKING FOR BLEEDING ESOPHAGEAL VARICES ASSOCIATED WITH PORTAL HYPERTENSION*

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Garlock[1], in 1947, reported the case of a young patient with bleeding esophageal varices. During an esophagoscopy a perforation of the cervical esophagus had occurred and an immediate mediastinotomy was performed with packing of the posterior mediastinum by means of iodoform gauze. This was followed by a mediastinitis which drained for several weeks. As an incidental postoperative observation, it was found that there was much less bleeding from the esophageal varices in this patient in the following six years up to the time at which the report was made.

Dr. Garlock theorized that this improvement may have been brought about by the formation of granulation tissue in the posterior mediastinum between the fibrosa of the esophagus and the prevertebral fascia which subsequently produced new vascular channels to divert the blood from the portal to the caval circulation. It was felt that the periesophageal veins could possibly carry the burden of the venous flow more efficiently than the submucosal veins thereby establishing a collateral circulation in veins not subject to easy trauma. The esophageal veins are located immediately beneath the mucosa of the esophagus and are only scantily supported by areolar tissue and are covered on the luminal surface by thinned out mucosa. Garlock, after reasoning as outlined above, decided to deliberately repeat the surgical procedure on the assumption that the irritation incident to the packing and infection would establish a collateral circulation in the mediastinum which might again result in improvement in patients having major hemorrhages from esophageal varices.

The operation was applied in a single patient in 1945 who had suffered recurring exsanguinating hemorrhages and who previously had undergone a splenectomy followed by many injection treatments of the esophageal varices without improvement in the clinical course. A cervical mediastinotomy was carried out and the esophagus was exposed in the superior mediastinum. The posterior zone of the mediastinum was opened bluntly and a finger was inserted down to the region of the arch of the aorta. The space developed in this fashion was packed freely with iodoform gauze and the packing was withdrawn slowly after eleven days. Esophagoscopy was carried out two months following operation and varices were found to be present. The patient subsequently suffered a major hemorrhage six months after operation and esophagoscopy at about that

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time showed that the upper three-fourths of the esophagus had returned to normal in appearance and that there were fibrotic varices about the cardia. There was no recurrence following the latter procedure during the fourteen month period of observation which has transpired up to the time that the report was made. Intermittent minor bleeding later supervened and in 1949 a thoracic mediastinotomy with packing about the mid and lower esophagus was performed.

In 1950, Garlock[2] reported further experiences in the use of this operation in a total of eight cases. This report indicates that none could be classified as having been cured of bleeding, however, there was improvement of variable degree in most of these patients in that the bleding was less frequent and less severe.

As one of the avenues of investigation of this problem, we have employed Dr. Garlock's operation in certain of those patients who are considered unsuitable for portacaval or splenorenal shunts. The reasons for so classifying these patients vary in typical fashion and include such causes as an unsuccessful effort at a shunt which may have been made elsewhere, the patient who has marked liver disease and is of advanced age and so forth. There have been eight who have fallen into this group and on whom the Garlock operation has been carried out. All of these patients were subjected to esophagoscopy and in every instance major esophageal varices were visualized. Seven of the patients were adults and one was a child. Only three have not bled at all since operation. One of these has been free of bleeding for four years, another for two years and the third for nine months.

Five patients in this group had recurring bleeding and in all but a single individual the hemorrhages were less frequent and distinctly less severe. Three of these five have since had additional surgical procedures. In all of these three patients, a second stage transthoracic packing of the mid and lower mediastinum was carried out along the lines indicated by Garlock and in two instances no subsequent bleeding has been noted. One of these patients, however, continued to bleed without improvement following both stages of the Garlock operation and was subsequently subjected to a transesophageal ligation of the varices with a totally unsatisfactory result. In this instance the varices could be demonstrated to be limited as far as one could ascertain to the lower third of the esophagus, therefore, it was decided to carry out a resection of the lower esophagus and to perform an esophagogastrostomy. This patient has now been absolutely free of evidence of bleeding for twenty-two months and it may be added that this is the first interval of freedom from hemorrhage that she has experienced in many years.

All five of the patients who have bled following the Garlock operation have been subjected to postoperative esophagoscopy on at least one occasion and in every instance varices are still present and insofar as could be determined they were without evidence of change. Three patients who have not bled since packing

of the mediastinum have not permitted a repeat esophagoscopy to date. No patient in this group of eight has died from any cause thus far.

Perhaps the most interesting case was that of a 58 year old white male, who was known to have advanced cirrhosis. There was a very marked ascites requiring repeated paracenteses. The liver function tests indicated definite impairment with 45 per cent bromsulfathalein retention and 4 plus cephalin flocculation test. Continuing severe hemorrhage required a total of close to 100 pints of blood over a thirty day period to maintain life and under the circumstances he was not considered a suitable candidate for one of the shunt operations. Therefore, the cervical stage of the Garlock operation was carried out in 1949. There was only one moderate episode of bleeding which occurred after operation and followed the ingestion of some potato chips on the seventh postoperative day. Following this he did not bleed for a period of two and one-half years although repeated esophagoscopy revealed the presence of very large varices throughout the entire length of the structure. In this interval the ascites disappeared and the liver function tests returned to normal levels. Two and one-half years following the operation the patient experienced his first hemorrhages and these were of only moderate degree and occurred over a period of five days during which he was hospitalized. He has again been free of bleeding for another period in excess of six months.

Summary

1. The use of the Garlock operation has been reported in 8 patients.

2. All patients reported have been subjected to esophagoscopy and have been shown to have major esophageal varices.

3. Three of these patients have not bled following operation.

4. Five patients have had subsequent hemorrhages and three of these patients have had additional surgery.

5. Five patients who have bled following packing of the mediastinum have all been examined by esophagoscopy and the varices were still present and appeared unchanged.

6. The three patients who have not bled since operation have not permitted the examination with the esophagoscope.

7. It is doubtful whether there is an interval of time of non-bleeding which will be acceptable as a guarantee of cure.

Conclusions

1. The Garlock operation has been carried out in 8 patients with fairly satisfactory results.

2. Further use of this operation and continued investigation of its possible role in our armamentarium are believed to be justified and are, therefore, encouraged.

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Discussion

Dr. Samuel Harbison (Pittsburgh, Pa.):—The presence of esophageal varices by esophagoscope—and that is the only certain way of being sure that they are or are not there—certainly isn't connected necessarily with the bleeding.

At least we can say for Dr. Payne and Dr. Kent that they are not lord high executioners, as are the rest of this panel today, because their mortality has been zero, one because she doesn't use the knife, perhaps, and the other because he uses it in a somewhat different position. In any event, I thought it would be interesting for five or ten minues, if you wish, to have the panel here at the table answer questions on this very clear, simple subject, from any of the audience who wish to participate. Please feel free to do so.

Dr. Hyman I. Goldstein (Camden, N. J.):—Sixty years ago Albert v. Mosetig-Moorhof of Vienna, first used intraperitoneal insufflations of oxygen as a therapeutic measure in pelvic and abdominal tuberculosis, as did also Wm. S. Bainbridge (during 1908-1922) of New York. Georg Kelling used (1901, 1910, 1913) pneumoperitoneum for diagnostic and therapeutic purposes as did also Alex. Lorrey, H. H. Carrelli, Haenisch, P. Rosenstein and Eugen Weber and others. Pneumoperitoneum has been of diagnostic aid in roentgenographic studies of intrabdominal lesions, with and without the use of peritoneoscopy and direct (under peritoneoscopic vision) biopsy. It has been used in the treatment of shock and hemorrhage as a tamponage. Oxygen insufflations have been used to prevent hemorrhage after extensive abdominal operations, and to prevent the formation of adhesions. Have the members of this panel had any recent experience (as a diagnostic and therapeutic aid) with pneumoperitoneum and with peritoneoscopy? Pneumoperitoneum has been used to stop hemorrhage from esophageal varix successfully and gastrointestinal hemorrhage of unexplained origin.

Dr. Harbison:—It is an exceedingly interesting question, which I shall address to the panel, and we are grateful for the information, because the only thing we have in acute stages of bleeding is the introduction of the rather brutal balloon. The patient Dr. Kent described had the balloon down successfully for some eight or nine days.

Would the panel like to comment on pneumoperitoneum?

Dr. Goldstein:—And the value of oxygen insufflation in relation to shock.

Dr Harbison:—Resulting from hemorrhage.

Dr. Goldstein:—That is right.

Dr. Mary Ann Payne (New York, N. Y.):—I would like to comment on the second point, the relationship of anoxia to liver failure and to hematemesis.

One cannot help but be impressed by the frequency with which clinical signs of liver failure precede bleeding. Conversely liver function is often further embarrassed following hemorrhage even to the point where jaundice and ascites occur. It would appear that portal pressure waxes and wanes with the state of the parenchymal cells and that even minor insults may be sufficient to cause a rise in portal pressure over the critical level for bleeding. Himsworth's work shows that anoxia is the factor responsible for the ultimate death of the cell in a wide variety of liver injuries. Therefore, measures to combat anoxia such as direct administration of oxygen as well as vigorous efforts to combat shock in the cirrhotic patient are definitely indicated.

Dr. Harbison:—That is, of course, very closely related to the present emphasis on the protection of the damaged liver by oxygen during all operations. The anoxia is perhaps much more important than we had realized in the past.

Do Dr. Madden or Dr. Lord have a comment on the alteration in portal hypertension, by the introduction of air into the peritoneal cavity?

Dr. Lord:—No comment.

Dr. Kent:—No.

Dr. Harbison:—You would be interested in trying it some time, Dr. Madden?

Dr. John L. Madden (New York, N. Y.):—I should just like to comment, if I may, but not to answer the question. I know nothing about it myself and have no experience with it. I think, however, we can answer many of the questions if we know what the basic pathologic physiology is.

I should like to show some slides related to the intrahepatic circulation.

As Dr. Payne brought out, we do not know too much about the intrahepatic circulation. Dr. Child has ligated the portal vein in the monkey as well as in the human, and no ascites has resulted. We know we can ligate the inferior vena cava below the renal veins therapeutically and yet we do not get ascites. We also know if we partially occlude the thoracic segment of the inferior vena cava we always get ascites. Also in chronic congestive failure ascites may occur.

What, then, is the pathogenesis of ascites? Apparently it is not due to extrahepatic portal bed block but to an intrahepatic disturbance of the circulation. Dr. Herrick showed that, gram for gram, the cirrhotic liver took more perfusion

fluid than the normal. Dr. McIndoe demonstrated an intrahepatic portal bed deficit. By this study we have confirmed both of them. Dr. Herrick is presumed partially correct, and Dr. McIndoe is presumed partially correct. Evidently Dr. Herrick was dealing with a cirrhotic liver with ascites, and Dr. McIndoe was dealing with a cirrhotic liver without ascites.

This slide shows the normal liver. The portal vein has been injected with yellow colored latex and the hepatic vein with blue colored latex. One can see the even distribution intrahepatically between the portal and the hepatic venous beds.

(Slide) This is the cirrhotic liver with ascites. Here there is an absolute and overall increase in the intrahepatic portal bed. One can see very little blue, as there is an almost complete obliteration of the intrahepatic venous bed, with a complementary overall increase in the intrahepatic portal bed.

(Slide) This is the cirrhotic liver without ascites, and one can see that there is a symmetrical deficit in both the intrahepatic portal bed and in the intrahepatic venous bed.

(Slide) This is the concluding slide which consists of a comparative study of the intrahepatic circulation in the normal liver, in the cirrhotic liver with ascites, and the cirrhotic liver without ascites. In the center is the normal liver showing the relation of the intrahepatic portal bed to the intrahepatic systemic venous bed. One will note the symmetrical distributions of both venous beds within the liver. On the left is the intrahepatic circulation in the cirrhotic liver with ascites. Here you may note the reciprocal pattern of the intrahepatic circulation characterized by a secondary and absolute increase in the intrahepatic portal bed and a marked decrease in the hepatic systemic venous bed. It is evident that in cirrhosis of the liver with ascites there is not an intrahepatic portal bed deficit, as Dr. McIndoe stated, but an absolute increase. Of course, this increase in intrahepatic portal bed would be in keeping with the perfusion studies of Dr. Herrick. On the right is the intrahepatic circulation in cirrhosis of the liver without ascites. In this, one sees the symmetrical pattern characterized by an absolute deficit in both the intrahepatic portal and the intrahepatic systemic venous beds. The deficit in the intrahepatic systemic venous bed, however, is not nearly as marked as that which occurs when ascites is present. This finding would agree with Dr. McIndoe's experiments. Thus we may presume from our own study that in the experiments of Dr. McIndoe he must of necessity have been dealing with the cirrhotic liver without ascites. We would also presume from our studies that of necessity Dr. Herrick, in contradistinction to Dr. Mc Indoe, must have been using livers of individuals with cirrhosis and ascites.

We have attempted to demonstrate that the pathogenesis of ascites in cirrhosis of the liver is not primarily an intrahepatic portal bed block. It is postulated that primarily it is an intrahepatic systemic venous bed block; that is, an obstruction of the outflow tract of the portal bed. True, there is an intra-

hepatic portal bed block but this is a secondary phenomenon to the primary blockage in the intrahepatic systemic venous bed. The compensatory increase in the intrahepatic portal circulation is nature's attempt to overcome this blockage of its outflow tract. Accordingly, in the treatment of cirrhosis of the liver with ascites, the use of an extrahepatic portacaval shunt would be absolutely contraindicated. By doing such an operation you would produce a complete and sudden decompensation of nature's mechanism to compensate for the existing intrahepatic obstruction of the systemic venous bed.

Dr. Harbison:—Now, I hope you are sufficiently confused. But that is the only way we will ever get at this problem. I think that is very brilliant work. We are just beginning to try to duplicate this sort of perfusion experiment, and try to find out what goes on in the liver. The trouble is that we are using dead livers. We can't do this work very well with the live patient.

If I might summarize anything today, it is that the treatment of bleeding esophageal varices in cirrhosis of the liver must eventually be a medical problem of prevention; that during the interim when we are not able to cure these patients or ameliorate them, or help them, we turn to surgery, and perhaps surgery's greatest contribution to this subject has been the elucidation of some of these physiologic and pathologic observations which some day may help in the final evaluation and treatment of the disease; but certainly we, as surgeons, are not under any delusion that we are accomplishing anything more than supplying a temporary measure for the treatment of symptoms.

PRESENT STATUS OF RADIOISOTOPES IN GASTROENTEROLOGY*

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As was stated a dozen years ago[1] radioisotopes will play a much greater role in the diagnosis rather than in the treatment of hematological diseases. This statement also applies to gastrointestinal diseases.

Radioisotopes

Practically all elements can be made to be radioactive—i.e. give off rays like radium—with the aid of cyclotrons, linear accelerators, uranium piles, bevatrons, etc. Some of these radioactive elements discharge alpha rays that penetrate less than 1/10 mm. of tissue. Others discharge weak beta rays that penetrate less than 1 mm. of tissue, and still others emit gamma rays, that can penetrate several inches of lead. Some of these isotopes discharge their rays for only a few seconds and others for several years. Radium discharges alpha, beta, and gamma rays and has a half-life of 1600 years. A half-life is the time that it takes for a given quantity of discharged radiation to be reduced by one half. Before 1940 we knew of only 92 elements, but now we have 98 elements—the last 6 being man-made. At the present time, there are over 500 radioactive isotopes of these 98 elements. Most of these isotopes can be chemically incorporated into molecules of practically all substances known.

Radiation Effects

As is well known, different rays (alpha, beta, gamma, x-rays, neutron, ultraviolet, etc.) can cause many different types of cellular reactions. Some rays are lethal to cells, while others can cause mutation of cells; still others can cause intracellular changes such as the inhibition of enzymes (Dr. Hollander inhibited release of HCl by intracellular chemical inhibition) or the fragmentation of chromosomes, and still others can cause changes that make the cell involved secrete abnormal secretions, and finally there is evidence that radiations may result in neoplastic change:

1. Radiologists develop leukemia 10 times more frequently than other physicians[2]; 2. there is also evidence that there is increased incidence of leukemia in the Hiroshima population which was exposed to the atomic bomb[3]; 3. osteogenic

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sarcoma has been known to follow x-radiation therapy for nonmalignant lesions[4]; 4. sarcoma of the liver has occurred following the injection of thorotrast[5].

One of the most recent theories to explain the onset of cancer is that normal cells are converted into "latent tumor cells" by carcinogens (abnormal metabolism of cholesterol or other sterols or the ingestion of burnt cholesterol, etc.) and then precipitated into cancer cells by the later added insult of radiations, viruses, and other irritants.

Radiation Effects Upon the Gastrointestinal Tract

Similarly radiations have many cellular potentialities in all parts of the body including the gastrointestinal tract. For example, there are several reports and numerous pictures of the effects of the atomic bomb irradiation upon the gastrointestinal tract of the human victims[6,7]; and also those workers who were accidentally exposed to lethal doses of neutron rays[8]. In general it can be stated that after intense irradiation (including x-radiation to the body) the mucous membranes of the gastrointestinal tract become edematous, later hemorrhagic, and then secondary infections set in causing ulcerations, desquamations, and diphtheria-like necrotic membranes. The very first cells, however, that degenerate and disappear following irradiation of the intestinal tract are the lymphocytes, particularly those in the submucosa and in the Peyer's patches. Next in order of degeneration are the mucosal and glandular cells which undergo various types of degeneration, as stated above, and include vacuolization of both nuclei and cytoplasm. The nuclear distortions, known as "owl's eye" nuclei, are characteristic of irradiated cells. The muscle cells are usually not damaged.

Many years ago I was interested in the lymphocytes of the gastrointestinal tract[9] and was convinced, as were many others, that most of the lymphocytes that float in the blood stream are made in the submucosa of the gastrointestinal tract; and now it is felt that the majority of all the leucocytes are probably destroyed in the lungs[10,11]. I later learned[12] that by making dogs swallow a small rubber balloon containing radioactive phosphorus the asbolute lymphocyte level in the blood stream dropped precipitously while an equal amout of irradiation from radioactive phosphorus applied to the skin did not cause a significant drop. This would imply that a small amount of irradiation to the gastrointestinal tract causes a more profound lymphopenia than when an equal amount of irradiation is applied to the skin. Some of the dogs developed sigmoidal and rectal ulcerations which later bled slightly probably due to the fact that the balloons moved less rapidly in these particular areas and, therefore, resulted in more irradiation of the mucosa; and possibly in secondary telangiectasia.

In general, radiations directed from the exterior of the body or when applied from within the lumen of the gastrointestinal tract will cause lymphopenia due to the loss of the lymphocytes that are produced in the gastrointestinal tract; and this can be followed by ulcerations of the gastrointestinal mucosa.

Radioisotope Therapy

Internal irradiation can be used as a method of therapeutic irradiation. Technically it would not be too difficult to fill the bag of the Miller-Abbott tube with a beta ray-emitting solution of some isotope such as radioactive phosphorus. The site for the localization of the bag could be determined by instilling barium through the other lumen of the tube. Therefore, beta irradiation which penetrates only a few mm. of tissue could be applied to a lesion almost in any part of the gastrointestinal tract. Beta irradiation of rectal lesions are now possible also by the use of various balloons or needles and even plastic hollow threads containing such isotopes as radiocobalt. One could use isotopes which emitted stronger beta rays or even gamma rays (CO^{60} or Au^{198}).

The radiation of a gamma-ray producing isotope could be used as a source for taking photographs from within the lumen of the gastrointestinal tract. No electric wires and no complex equipment would be necessary. Radioactive thulium 170 has been used experimentally at the present time[13]. Undoubtedly, this technic will require many years of development, but it is an interesting application of isotopes.

Radioactive agents can also be instilled into the peritoneal cavity. For many years solutions of radioactive gold have been used intraperitoneally[14] to control ascites caused by peritoneal implants or even metastatic disease to the liver. Obviously, there are all degrees of success depending upon the type and location of the malignancy, the general condition of the patient, the sensitivity of the involved malignancy cell to radiation, etc. Ascites in many patients with metastatic peritoneal cancer, however, can be controlled temporarily or satisfactorily for months at a time, with radiogold.

Indirectly, of course, various gastrointestinal lesions which occur in patients with polycythemia and leukemia can be overcome or controlled at least by radioisotopes since the radioactive isotopes cause remissions of the polycythemia and leukemic processes. For example, gastrointestinal bleeding is not too uncommon in polycythemia because of the presence of too much viscid blood. Since radioactive phosphorus causes remission of the polycythemia the gastrointestinal bleeding is thereby indirectly controlled.

Diagnostic Aspects of Radioisotopes

The more important aspects in the future in regard to diseases of the gastrointestinal tract and isotopes are the diagnostic features. For example, Cayer and Cornatzer[15] were able to discover by the use of radioactive phosphorus that lipotrophic factors were of clinical value in patients with fatty livers and of no particular value in liver diseases in which there was no fatty infiltration or degeneration. Other investigators[16] have learned that patients with cirrhosis

metabolize albumin much more slowly than normal individuals. They were able to come to this conclusion by the use of albumin tagged with radioactive iodine. Schulman et al[17] have demonstrated an increased phosphorus turn-over in carcinoma of human stomachs. These stomachs, of course, were obtained from surgical specimens. But this type of information perhaps could be made practical for diagnosis. It seems to me that it would not be difficult to swallow a small Geiger counter placed within the lumen of a Levine tube. With the aid of a gastroscope one could apply the Geiger counter directly upon a lesion of suspicious character (if the lesion was within the limits of the gastroscopic field). One could then inject radioactive phosphorus intravenously and note the uptake in the involved mucosa and in normal mucosa. Of course, many problems in geometry would have to be worked out. But since one can suspect skin cancer, breast cancer, and testicular cancer, which are located close to the body surface, by the differential uptake of radioactive isotopes, particularly P-32, there is no reason to think that stomach cancers could not likewise be diagnosed by similar technics. In those cases where it is very difficult to perform satisfactory biopsies of the gastric mucosa with the aid of a gastroscope, such isotope technics might be applied.

Other investigators[18] have shown that radioactive phosphorus is picked up in the desoxyribonucleic acid fraction of the nuclei of liver tumors of animals in concentrations 25 times greater than in the normal liver cells. This differential uptake of isotopes in malignant cells has great diagnostic potentialities, even in liver aspiration biopsies with special Geiger counters. Similar differentials in the desoxyribonucleic acid content of human leukemic cells has also been noted[19]. Another relationship between gastroenterology and hematology is the use of radioactive Vitamin B_{12} (the cobalt molecule is made radioactive) as a test for the intrinsic factor activity of various substances such as hog stomach and gastric juice. Seventy-five to ninety per cent of the orally administered radioactive Vitamin B_{12} is excreted in the feces of patients with pernicious anemia when no gastric juice is simultaneously administered; but only 5 to 30 per cent is excreted when gastric juice is administered[20].

Perhaps the most important fact to gastroenterologists is that carbohydrates, fats, proteins, various minerals (sodium, potassium, calcium, iron, etc.), vitamins, hormones, and even bacteria can be labeled with radioisotopes. The metabolism of these agents and their effect on the metabolism of the body can be better understood thereby. It was rather startling to me years ago to learn that up to 33 per cent of the carbon of fats and proteins is exhaled from the lungs very shortly after eating labeled food. It seems unpleasant that after one eats a nice juicy steak that one blows off 30 per cent of it as CO_2 into the air within an hour or two. Now we can better understand why garlic breath comes from the lungs. This was a rather vitriolic subject some 15 years ago[21]. Most investigators had felt that garlic and onion breath was due to retained particles between the teeth, but now we know that it does come from the lungs.

Fats

Stanley and Thannhauser[22] have shown that humans who orally received olive oil labeled with I-131, discarded some by way of the lungs, stored some in adipose tissue, incorporated some into phospholipids, etc. Lerner et al[23] came to the same conclusions by administering intravenously palmitic acid labeled with C-14. Chaikoff[24] presented in 1942 a most complete review of phospholipid metabolism by the use of labeled agents.

Proteins

The fate of methionine[25] in various diseases has been studied by labeling it with sulfur-35. S-35 was first incorporated into plasma protein. After the intravenous administration, there was a significant deviation from the normal excretion rate in patients with chronic liver disease, with hypoproteinemia, or with Cushing's syndrome. When methionine was labeled with deuterium, du-Vigneaud[26] showed that methionine furnished methyl groups for the synthesis of choline and creatine. He also indicated that betaine supplied methyl groups for creatine production. Mackenzie[27] also showed that the methyl groups of methionine ultimately became incorporated into the porphyrin molecule which of course becomes hemoglobin later.

Minerals

Harrison and Harrison[28] showed that in rats most rapid absorption of calcium occurs during the first 2-4 hour period following ingestion and in the proximal portion of the small intestines. The rate of absorption is not influenced by Vitamin D. Vitamin D increases absorption of calcium-45 only when there is a deficiency of calcium in the intestinal contents or when it is poorly soluble. Under these conditions calcium can be absorbed even from the distal intestines.

Carbohydrates

I won't discuss carbohydrate metabolism with labeled molecules since there are books written on the subject. Olsen[29] has indicated that labeled carbohydrates are treated differently in normal than in tumor tissues. For example, normal liver glycogen presumably is synthesized from blood glucose and lactate, then stored and resecreted as glucose. But in rat hepatoma no glycogen is stored and the hexokinase and the phospho-hexokinase are more active in the tumor cells.

Miscellaneous

Tabern et al[30] have listed and discussed some 25 drugs that have been labeled so far. They also list 10 amino acids, 5 vitamins, 5 dyes, 5 alkaloids, 5 carcinogens, 5 hormones, and 10 biological materials, and 25 miscellaneous compounds that have been used experimentally in various ways. It would seem that almost every

agent can be made radioactive. Or perhaps I should say one or two atoms of each molecule can be made radioactive.

Conclusions

I think all of us know that the most important study for the advancement of medicine and for the understanding of disease in the future rests in the subject of intracellular chemistry. If we only knew the intracellular chemistry of the cells of the body, we undoubtedly could explain most of the problems that are bewildering at the present time such as cancer, insanity, arteriosclerosis, etc. Radioisotopes at the present time constitute the most accurate method of measurement of the intracellular reactions.

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THE POSTCHOLECYSTECTOMY SYNDROME*

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The problem designated as postcholecystectomy syndrome has appeared frequently in medical literature within the past fifteen years. It may be defined as the presence of any of a group of symptoms occurring after the removal of the gallbladder. These include: pressing or colicky pains in the right upper quadrant, pain under the right scapula or above the right clavicle, anorexia, nausea, flatulence, weight loss, diarrhea, constipation, chills, and fever. All too often, the postcholecystectomy patient has symptoms which he thought would be eliminated by operation, or which he now believes to have been caused by the operative procedure. Twenty years ago, the etiology of such symptoms was most often thought to be spasm of the sphincter of Oddi. This concept stemmed from Oddi's original work which showed that there was hypertrophy of the bile ducts following cholecystectomy[1].

We know now that many other important factors enter into the postcholecystectomy syndrome. In visits that the author made to European clinics in 1952, which included several surgical and gastroenterological conferences, these factors were discussed and studied. The Gastroenterology Congress at Santander, Spain, devoted most of its time to the evaluation of postcholecystectomy syndrome. It was formulated in many European clinics, that a large proportion of unsatisfactory results after cholecystectomy are attributable to incomplete preoperative study. Many other unsatisfactory results are attributable to inadequate study of the abdominal organs at the time of operation. There follows a table of classification of causes of the postcholecystectomy syndrome.

TABLE I

POSTCHOLECYSTECTOMY SYNDROME

1. Erroneous preoperative diagnosis
2. Calculi in the common duct or hepatic ducts
   a. Residual
   b. New formation of calculi
3. Calculi in the cystic duct.
4. Incomplete removal of the gallbladder with dilation of the stump and formation of a "new gallbladder"
5. Cholangitis
6. Ductal stricture
   a. Primary
   b. Operatively produced
7. Adhesions involving stomach, duodenum, or other intestines

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8. Bacterial infection of the duodenum
    a. Primary
    b. Operative etiology
9 Hepatitis
    a. Residual
    b. Operatively produced
10. Metabolic disturbances with "hepatolithiasis" or "dripping of stones"
11. Pancreatitis
    a. Residual
    b. Operatively produced
12. Reflux of bile into the pancreas
13. Endocrine deficiency of hormone secreted by gallbladder
14. Deficiency of lipase production of pancreas
15. Compression of common and hepatic ducts by diseased surrounding organs, "perivisceritis" (e.g. pancreatitis)
16. Biliary dyskinesia
    a. Spasm of sphincter of Oddi
    b. Hypertrophic sphincter of Oddi
    c. Hypotonic sphincter of Oddi
17. Anomalous ducts
18. Removal of a normally functioning gallbladder
19. Neoplasms of liver, biliary ducts, or pancreas
20. Postoperative psychogenic trauma
    a. Psychosomatic states
    b. Postoperative asthenia
21. Wound pain (e.g. ventral hernia)
22. Pain of neuroma adjacent to amputated cystic duct

Preoperative Study

It must be known preoperatively whether or not the gallbladder functions normally, if one is to eliminate a large number of the causes of postcholecystectomy syndrome.

A normal gallbladder concentrates and stores bile, which it delivers into the duodenum as food is injected. The bile aids in digestion, particularly in the absorption of fats. Other functions of the gallbladder include production of mucus and a hormone. Pribram has named the hormone "cholecystmon". He showed that bile from the gallbladder, which contains the hormone, had more digestive action on milk and other foods, than did bile from the hepatic ducts. Cholecystmon is now in the process of being commercially prepared for clinical use. It acts to stimulate production of pancreatic lipase[2].

Removal of a functioning gallbladder may give rise to symptoms due to lack of this bile reservoir, as there is a continuous draining of bile into the intestines which results in diarrhea and postprandial distress. These symptoms may pass, in several days to a few weeks, as the storage function is taken over by the ducts. Oddi suggested that spasm of the smooth muscle at the ampulla of Vater produced back pressure and dilatation of the ducts with later production of a bile duct reservoir[1]. That concept immediately suggests two etiologies of the postcholecystectomy syndrome: 1. spasm of the sphincter causing pain, 2. failure of the sphincter to contract so that there is no reservoir of bile. These examples of dyskinesia are but two of many causes of the postcholecystectomy syndrome as shown in the table of classification.

Cholecystography and Transduodenal Drainage

It is the accepted procedure in many European Clinics, especially the Western European Clinics, that preoperative study include both cholecystography and transduodenal drainage. At the 1952 Convention of Mediterranean and European Gastroenterologists, the apparent international loss of popularity of duodenal drainage was discussed. The recent significant work by Lopez[3] and others has helped repopularize transduodenal studies in Europe. His work definitely established that a pain pattern may accompany a peroid of closure of the sphincter of Oddi. He also showed that diagnostically and therapeutically, novocaine may relax the sphincter of Oddi when placed in the duodenum through a tube. Duodenal drainage studies to diagnose dyskinesia would prevent one cause of postoperative recurrence of symptoms.

Cholecystography which does not reveal a gallbladder outline does not necessarily indicate a nonfunctioning gallbladder. In liver disease, the dye may not concentrate in the biliary tract, or a patient may be too obese for one to see the concentration. Even when a large dose of dye (e.g. a "double dose" of priodax) is used, and a nonfunctioning gallbladder is diagnosed, it is worth repeating the x-rays in two weeks. Often, after a regimen of good diet and bowel elimination, the cholecystograms appear normal. Albot, et al[4] have pointed out that cholecystograms should always be taken in AP and lateral views, as well as erect and horizontal.

Examples of Erroneous Preoperative Diagnoses

There are many diseases which may simulate gallbladder disease and which might lead to needless cholecystectomy unless proper diagnostic steps are taken.

Coronary disease is known to be related to gallbladder disease, in that one may simulate the other, and in that occurrence of both diseases together is common[5]. The pain pattern may be only slightly different, with angina radiating into the left arm or shoulder, and gallbladder disease giving pain in the right shoulder. A careful history, an x-ray of the heart, or electrocardiogram, and an exercise tolerance test should help prevent removal of a normal gallbladder. If both organs are diseased, however, cholecystectomy may improve the angina pectoris.

Stomach and duodenal disease may simulate gallbladder disease. These diseases may include: gastric neoplasms, peptic ulcers, cardiospasm, pylorospasm, duodenal diverticuli. Pancreatic infections, neoplasms, and calculi have been known to simulate biliary disease. Renal diseases, especially calculi, mimic gallbladder trouble. Peritonitis, appendicitis, liver diseases should also be considered.

The author had the opportunity in 1952 to review the study of 1,000 cases of postcholecystectomy syndrome done by G. F. Bonnet, at Vichy, France. It was found that 66 per cent of these cases had probably had erroneous preoperative diagnoses. The most common errors were psychogenic and vagotonic imbalances,

with intestinal disturbances such as spastic colitis, and dilated cecum with increased carbohydrate formentation.

Hiatus hernia and epigastric herniae, are conditions which have simulated gallbladder disease. Epigastric herniae and postoperative incisionl herniae have proved fairly common in the author's experience as causes of postcholecystectomy pain. There follows a table of conditions which simulate gallbladder disease.

TABLE II

ERRONEOUS DIAGNOSIS

1. Coronary disease
2. Gastric diseases: neoplasms, gastritis, peptic ulcer
3. Duodenal diseases: diverticuli, infection, ulcer
4. Pancreatic diseases: neoplasms, infection, calculi
5. Renal diseases: neoplasms, infection, calculi
6. Liver diseases and hyperemia
7. Vagotonic imbalance intestinal disturbances
8. Appendicitis
9. Peritonitis
10. Retroperitoneal tumor
11. Spinal arthritis

OPERATIVE STUDY

Careful exploration of the abdomen and special study of the biliary system during cholecystectomy would eliminate several other causes of the postcholecystectomy syndrome. Study of the ducts is concerned both with calculi and disturbances of the sphincter of Oddi. Lahey[6] stated that 25 per cent of cholelithiasis cases also have calculi in the common or hepatic ducts. He has argued for exploration of the common-duct whenever there is any suspicion of choledochelithiasis. Mallet-Guy[7], of France, found in 100 consecutive cases of cholecystectomy that 38 had diseased ducts. These cases were found by routine cholangiography on the operating table and routine manometric studies during operation. A pressure in the common-duct of 7 mm. of mercury or more (with spinal anesthesia) was considered diagnostic of an obstructed ampulla of Vater.

The author, in his visits to European Clinics, was very favorably impressed with the work of Mallet-Guy and others on manometric study and cholangiography. The exhibitions at the Congress of Surgeons in 1952 in Paris contained many fine operating tables specially constructed for cholangiography. The careful operative study seen in France and in other western European Clinics was in contrast to the blind probing of common ducts done in Clinics to the East. Also, in the West, the transduodenal exploration of the ampulla of Vater was done more frequently.

Operative study cannot be so complete in operations for acute cholecystitis. Often, inflammed tissues make dissection and exposure difficult and even dangerous. This fact is unfortunate in view of the increasing tendency to do cholecystec-

tomies for acute cholecystitis. Cholecystectomy or medical management in more cases would mean better operative study at a later date, with less chance of the postcholecystectomy syndrome. Medical treatment is safer now than in the past because of antibiotics, electrolyte control, transfusions and Wangensteen decompression. Proper conservative care could reduce the operations for acute cholecystitis to a minimum.

Involved in the operative study, but more a problem of the technic of cholecystectomy, are two other commonly reported causes of postcholecystectomy syndrome. Diseased gallbladders usually have diseased cystic ducts which should be removed as completely as possible. A long cystic duct stump is subjected to a new increased backpressure, postoperatively. The diseased duct has no power of expulsion and stasis results. This, together with any nidus of postoperative infection, may result in the formation of a stone in the cystic duct. Also, infection alone, in long cystic duct stumps may give postoperative symptoms. A similar cause of postcholecystectomy syndrome is the incomplete removal of the gallbladder so that the remaining stump becomes dilated.

The study at operation, of course, should include an adequate abdominal exploration through an adequate incision. The colon, stomach, liver, right kidney, pancreas, and duodenum should all be examined carefully.

Postoperative Factors in the Postcholecystectomy Syndrome

Even with improved preoperative and operative study, some types of postcholecystectomy syndrome may still occur. Bile duct calculi which form after surgery are not necessarily the result of a long cystic duct or gallbladder stump. Calculi may form in the hepatic and common ducts postoperatively whenever there is a nidus of traumatized or infected tissue. This may take one year or twenty years. "Hepatolithiasis"[8] or formation of stones in the liver, may cause stones to drop down into the larger ducts. "Hepatolithiasis" is due to improper cholesterol metabolism in the liver cells. Treatment includes a low fat diet and high fluid intake. Bile salts and the newer antibiotics should be administered.

When a common duct is opened and calculi are removed, further calculi may be discovered with repeated postoperative cholangiograms through a T-tube. Removal of the tube would lead to the postcholecystectomy syndrome. Rather than immediate reoperation, one should first try the Pribram Method[9] of ether instillations to dissolve the calculi.

Reflux of bile into the pancreas is thought to cause a chemical pancreatitis. The reflux may be due to obstruction by spasm, stone, or other occluding lesions at the ampulla of Vater. Following cholecystectomy another etiology of reflux of bile is present, if one again accepts that there is increased pressure in the common duct after cholecystectomy. Thus, a postoperative pancreatitis of varying severity may occur. A very mild pancreatitis may explain the transient glucosuria often seen after cholecystectomy. Severe pancreatitis may be difficult to treat, and it may

give recurrent abdominal pain, and later steatorrhea, diarrhea, and even diabetes mellitus. Medical treatment is mainly symptomatic and supportive with administration of pancreatin in some cases. Surgical treatment may involve major procedures including: sympathectomy, pancreatectomy, or pancreatico-doudenectomy. This latter procedure removes the site of obstruction at the ampulla of Vater and also the diseased tissue of the pancreas[10].

Diminished pancreatic lipase production has been observed after cholecystectomy in up to 71 per cent of cases. Either pancreatic changes or absence of Pribram's "cholecystmon" could account for this. "Cholecystmon" from the gallbladder wall is believed to stimulate lipase production[2].

Postoperative infections, when causing the postcholecystectomy syndrome, are not easily cured. A preoperative infection can be stimulated by operation, and for that reason it is well to treat biliary infections preoperatively if possible. The coliform organisms actually seem to become more virulent after cholecystectomy. With duodenal drainage, it is possible to do sensitivity cultures of the organisms and then select the proper antibiotics. Postoperatively, the bile ducts, the duodenum, or the liver may be infected. A "perivisceritis" has also been described[11]. In a necropsy series, Bryant[12] found that all cases who had had cholecystectomies possessed adhesions in the subhepatic area. "Perivisceritis" may be a clinical entity and adhesions may fix the stomach or duodenum and liver together, but one should exclude all other causes of the postcholecystectomy syndrome before a lysis of adhesions is attempted.

A bacterial hepatitis in some degree probably follows most gallbladder surgery. Hepatitis may be a difficult diagnosis to make. In addition to the usual liver chemistries, the author feels that a galactose tolerance test and needle punch biopsy may be performed. Treatment is aimed at increasing the glucose content in liver cells by the intravenous administration of 50 per cent glucose, usually mixed with 20 units of insulin.

The remaining causes of postcholecystectomy syndrome are amenable to surgical treatment in varying degrees. The postoperative incisional hernia may be repaired. Neuromas may be excised with some success. Anomalous ducts present a challenge for meticulous surgical correction.

Summary

The postcholecystectomy syndrome consists of abdominal pains and digestive disturbances similar to those which were present before cholecystectomy. The reasons for the syndrome include: 1. Cholecystectomies done when actually diseases of other organs were giving the symptoms, 2. missed hepatic and common duct stones at the time of operation, 3. postoperative conditions including: biliary infections, new stone formations, and secondary intestinal and pancreatic disturbances. The role of painful spasm of the sphincter of Oddi is no longer felt to be the leading cause of the postcholecystectomy syndrome.

Elimination of many cases of the postcholecystectomy syndrome may be accomplished by: 1. preoperative diagnostic studies to make sure a functioning gallbladder will not be removed, 2. operative studies to discover the status of calculi in the bile ducts and the status of the ampulla of Vater, 3. operative exploration of the abdomen to rule out other unsuspected diseases, 4. proper treatment of some of the postoperative conditions which still are not eliminated by the previous mentioned measures.

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Discussion

Dr. I. Snapper:—Dr. Upham has brought up a problem which is of great clinical importance.

It seems to me that the postcholecystectomy syndrome develops most frequently in patients who are operated on without a correct indication. In patients suffering from pains in the upper right quadrant with a well-visualized gallbladder, usually no pathology is found at operation, even if the gallbladder empties slower than normal. There are exceptions to every rule, but in general a gallbladder which can be visualized should not be removed because these are the patients who later come back with postcholecystectomy syndromes.

When patients who actually had gallstones at operation develop a post-cholecystectomy syndrome, careful clinical investigation as depicted by Dr. Upham is necessary. If no other disease is found then usually common duct stones are present. Whether these stones have been left behind or have been caused by the surgeon, remains to be seen. There are many surgeons who, after

they have removed a gallbladder full of stones, allow their patients to eat everything, ice cream, liver, butter, lobster, and many other nutrients high in cholesterol. Such a diet will easily lead to the development of new stones. It should be stressed that removal of the gallbladder does not remove the disease which caused the formation of stones in the gallbladder. Thus a patient who has had gallstones has to follow a careful diet even after operation.

Among the other causes for a postcholecystectomy syndrome Dr. Upham has rightly emphasized the presence of chronic pancreatitis. It is regrettable that often after the cholecystectomy the pancreatitis still persists.

A third complication is hemorrhagic gastritis. After a cholecystectomy, occasionally hemorrhagic gastritis develops which may continue for many months, sometimes for many years. Every patient with an unexplained postcholecystectomy syndrome requires a gastroscopy to exclude this hemorrhagic gastritis.

Dr. Wangensteen:—I agree with Dr. Snapper concerning the indications for cholecystectomy. They should be a good deal more rigid, I think, than they sometimes are in practice. Cholecystography, of course, helps a great deal in the diagnosis of gallstones; however, it did result in liberalizing some of the indications for cholecystectomy. Many surgeons remove the gallbladder in patients in whom no stones are demonstrated, but in whom some malfunction or filling or emptying is present, such that the gallbladder shadow didn't show. I know of a pathologist who lost his job in a voluntary hospital in our area because he diagnosed these non-stone containing gallbladders as normal—too often in the experience of the surgeons who removed them. Well, it takes time to accept unpleasant decisions. I presume those surgeons too now have capitulated to the thought that their victim was innoncent.

A number of years ago, this Course was held in another city. There was a surgeon there who talked about indications for cholecystectomy, and they were very liberal indeed; included amongst others was fatigue. In fact as I remember it, he exhibited himself as testimony of how successful cholecystectomy can be in the relief of fatigue. So I said to him, "In my area there is a man who takes out the gallbladder on the very slightest indication, and they call him Gallbladder B—. They don't by any chance call you Gallbladder S—, do they?" Those of you who were there will remember the hilarity with which this remark was greeted. I am afraid I lost a friend in the exchange.

Now, the postcholecystectomy syndrome does occur even in patients who have the gallbladder out on good indication. I wish Dr. Snapper would acquaint himself with the writings of my colleague, Dr. Boyden, concerning the sphincter of Oddi. Boyden and Schwegler demonstrated beyond the slightest suggestion of any doubt, by the reconstruction method, that the sphincter of Oddi is real. There can be no doubt about it.

Dr. Snapper:—I will be back in ten years.

Dr. Wangensteen:—No, Dr. Snapper, this is fact—not fiction.

Now, about the postcholecystectomy syndrome—I agree with what Dr. Upham has said, that in many instances perhaps a small stone has been left in the terminal common bile duct; however, there are patients in whom at secondary operations undertaken for the relief of this distracting and disconcerting syndrome, no stones were found. The cause of these painful postcholecystectomy syndromes is not known. A number of operative procedures have been employed to relieve these painful attacks of biliary colic.

In recent years I know of a T-tube being put in the common duct and left there for a long time. A rabbi, a well-known man here in New York now, had a number of such operations without relief, and he was at the point of despair, in the slough of despondency. I put a tube in his duct and left it there for over a years. I have seen him now many times, and it must be eight years since his operation. He is perfectly well. There are, however, as Dr. Upham suggested, better technics.

There is the technic devised by Archibald and Doubilet. Some of you are familiar with the passing of the Bockus dilator down the common duct. If it meets with the slightest resistance, the surgeon should restrain himself and not push on it. There is the McBurney duodenotomy, with cutting of the sphincter over a guide in the lumen of the common duct. When the surgeon meets with a suggestion of resistance in pushing a dilator down the common bile duct, I do believe the best thing to do is to perform McBurney's duodenotomy, guiding the probe in the duct under direct vision. Occasionally a stricture will be found there.

I think one should abandon attempts at slitting the terminal ampulla with the Archibald-Doubilet knife. It is preferable to do it with a knife through a McBurney duodenotomy incision. My experience with this method has been very satisfactory.

There is another technical consideration I would like to mention, viz; the technic of assuring oneself that the common duct has been freed of stones. This technic has been very helpful, particularly in the presence of soft stones. I pass a small Bockus dilator down the common bile duct and out through the exposed ampulla. A small French urethral catheter, usually a No. 14, is tied to the Bockus dilator and is pulled with the eye-end out through the opening in the common bile duct. The mouth-end of another No. 14 French catheter is sutured over the eye-end of the first catheter. I then make a tie, with baby-umbilical tape, in one or two places over the last catheter. Many soft stones which have eluded detection have been removed as these catheters are pulled out into the duodenotomy wound. It is, I believe, a simple and effective manner of cleaning out the common bile duct. Moreover, the method makes the taking of cholangiograms on the operating table unnecessary.

SUBMUCOSAL GASTRIC HEMATOMA: COMPLICATION OF THE VACUUM-TUBE BIOPSY TECHNIC

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and

VERNON M. SMITH, CAPT., M.C.

Washington, D. C.

Specimens of gastric mucosa obtained by the vacuum-tube technic[1] have proved of value for critical microscopic study because they are largely free of artefact. The safety of the vacuum-tube instrument depends on the absence of external moving parts and on the fact that it can excise only tissue which has been drawn within its lumen. The instrument (Fig. 1) consists of a 65-centimeter Fr. 30 rubber tube fitted at one end with a closed metal cylinder. A circular aperture four millimeters in diameter opens into the side of the cylinder. A sharp-edged metal piston can be drawn through the cylinder to shear off the knuckle of mucosa which is sucked through the aperture when vacuum is created by syringe at the other end of the tube. Normal mobility of the mucosa over the muscularis propria limits the depth of excision to the full mucosal thickness plus a small amount of underlying submucosa. The specimens are uniform mucosal discs measuring approximately 4 x 6 x 1.5 mm.

In this clinic gastroscopic examination routinely follows the biopsy procedure, to permit correlation between gross and microscopic appearances of the mucosa. The biopsy site appears as a dark red oval measuring approximately 4 x 5 mm. Difficulty at times experienced in visualizing this easily-recognized lesion gastroscopically has emphasized the common impression that important mucosal areas may remain hidden during a gastroscopic examination confidently considered to be complete. No significant postbiopsy bleeding has been encountered. Indeed, it has been a rare experience to find blood in the mucus lake or on the mucosa to facilitate location of the biopsy site.

Of the first 500 vacuum-tube biopsies performed in this clinic, two were complicated by the development of a submucosal hematoma. There have been no other complications. A brief description of the two cases follows:

Case 1:—A 46 year old white man was hospitalized with complaints suggestive of acute infectious hepatitis, and physical examination, liver function studies and liver biopsy confirmed the diagnosis. His course was a slow one, and serial liver biopsies showed progression to chronic hepatitis and, eventually, to early posthepatitic cirrhosis. Upper gastrointestinal roentgenologic studies were normal.

Routine gastroscopic examination seven weeks after the onset of illness showed generalized atrophic gastritis, with a particularly prominent submucosal

From the Gastrointestinal Section, Walter Reed Army Hospital, Washington, D. C.

venous pattern over the anterior wall and greater curvature. No other disease was found. No biopsy was taken at that time.

The second gastroscopic examination was made three weeks later, immediately following vacuum-tube biopsy. Although the general configuration of the stomach was normal, there was a discrete intramural swelling on the anterior wall of the mid-pars media, about one-third of the distance from the greater curvature to the lesser. It was a symmetrical ovoid, measuring about 2 x 3 cm., and elevated the mucosa perhaps 1 cm. into the lumen. The overlying mucosa was entirely smooth, and its color was similar to that of the rest of the mucosa. The regional rugae ended abruptly about the base of the lesion. The biopsy site was found over its distal end, without demonstrable surrounding reaction.

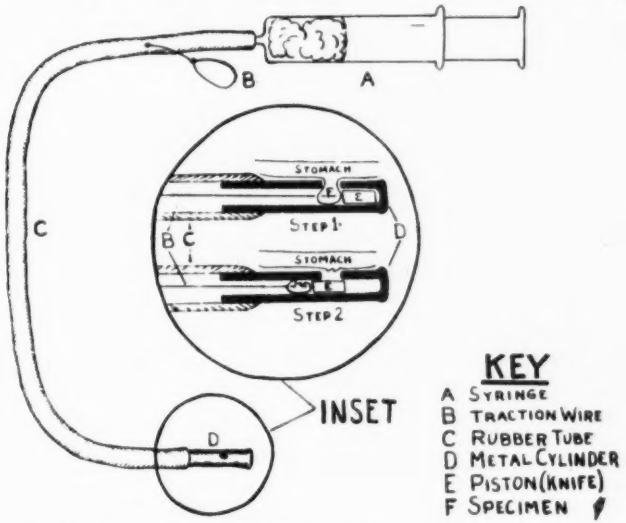


Fig. 1—Vacuum-tube biopsy instrument with cut-away view of the working parts. The metal cylinder is introduced into the patient's stomach. Vacuum is created within the metal cylinder (D) by syringe (A), step 1. This momentarily aspirates a knuckle of mucosa (F) into the cylinder. At this instant, the traction wire (B) is withdrawn, step 2, pulling the piston knife (E) across the aperture and shearing the specimen (F) off within the metal cylinder.

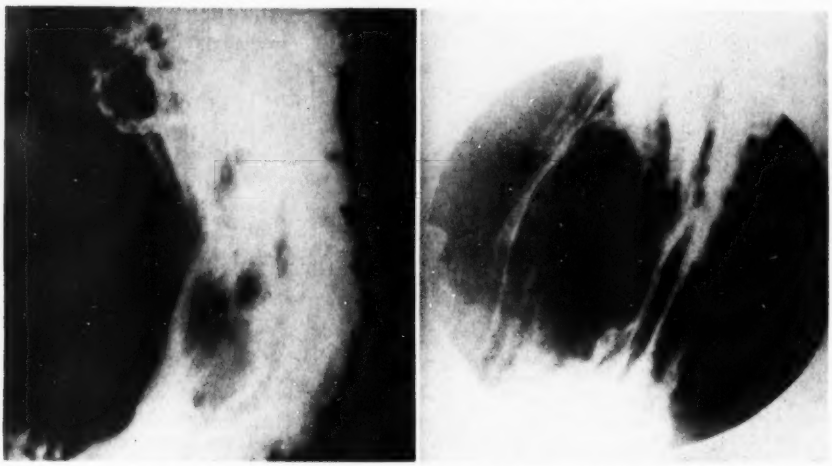
From the mucosal defect a thin curtain of clotted blood spread toward the mucus lake. The lesion was considered to represent a postbiopsy hematoma.

The next morning, the roentgenologic picture was striking (Figs. 2 and 3) and suggested to the radiologist a benign intramural tumor. The biopsy revealed moderate atrophy, intestinal metaplasia, and foci of round-cell infiltration. Most important, the submucosal tissue was composed largely of thick-walled arteries and arterioles. Meanwhile, the patient developed no symptoms referable to the stomach, and there was no external show of bleeding. Three and five weeks later,

at the third and fourth gastroscopic examinations, no evidence of the hematoma or any localized disease could be found.

Case 2:—A 32 year old white man was studied elsewhere because of chronic dyspepsia. Upper gastrointestinal roentgenologic studies were normal, and stools were free of blood. Achlorhydria was diagnosed, and the patient was referred for gastroscopy.

The stomach, examined immediately following vacuum-tube biopsy, contained no liquid or clotted blood. There was severe generalized atrophic gastritis. On the anterior wall of the mid-pars media, close to the greater curvature, there was an ovoid submucosal tumor, estimated to measure 3 x 5 x 1 cm. Although rugae approached the base of the swelling, its overlying mucosa was entirely



Figs. 2 and 3—(Case 1) Roentgenologic appearance of hematoma the day following biopsy.

smooth except for the dark purple biopsy site, which measured about 3 x 5 mm. The tumor's color was the same as that of the rest of the mucosa.

The biopsy specimen showed complete glandular atrophy with extensive round-cell infiltration. The submucosa was not noteworthy.

The patient was retained in the hospital for six days. Three stools were free of occult blood. He had no additional complaints following the biopsy and gastroscopic procedures.

On the sixth day, repeat gastroscopic examination showed that the hematoma was considerably broader, now measuring about 5 x 6 cm. It had become flattened, being elevated no more than the neighboring rugae. Its color again was entirely similar to that of the rest of the stomach. Its surface was smooth and intact, there being no residual evidence of the biopsy site.

The final follow-up examination was made three months after the first. The patient's dyspepsia persisted as before. There were no new facets to the problem. Gastroscopic examination showed generalized atrophic gastritis. There was nothing to suggest residuals or sequelae of the hematoma.

Comment

The mechanism whereby a submucosal hematoma may develop following mucosal biopsy is easily understood. Mobility of the mucosa, although contributing to the safety of the procedure, apparently may at times permit entrapment of a blood pool in the submucosa. Why only two of 500 cases were thus complicated is not clear. There was atrophic gastritis in each, but a casual relationship is not immediately apparent. One biopsy specimen included more than the usual concentration of submucosal blood vessels, but this is not necessarily a feature of atrophic gastritis.

No important sequelae were observed in the instances reported. The danger of intramural gastric hematoma is presumed to be that of secondary phlegmonous gastritis. It is probable that prophylactic penicillin would constitute judicious therapy following recognition of a hematoma in this location. None was used in these cases because the likelihood of local infection was not at the time considered great.

It is believed that iatrogenic gastric hematoma has not previously been described. It is not known whether the self-limited courses of the hematomas observed in these two cases should engender confidence in rather quick and uncomplicated spontaneous resolution, should the lesion be encountered in the future.

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EDITORIALS

Uremia and Gastointestinal Tract Ulceration

Of all the systems of the body, the gastrointestinal tract is characterized by the frequency with which ulceration occurs. Surprisingly, trauma is but an infrequent cause. These gastrointestinal ulcerations can be of either intrinsic or extrinsic origin. Peptic ulcer is distinctive and is of the former type. On the other hand, ulcerations of the extrinsic variety are more common than generally realized. Ulceration is prominent in blood dyscrasias. Out of 100 consecutive autopsies, 10 per cent had gastrointestinal ulcerations. This result occurred in a group of all types of deaths.

For a gastroenterologist, any disease causing ulceration is of paramount significance; especially if the pathogenesis is conceivably apparent. A clue to the etiology of peptic ulcer might be suggested. Such an excellent opportunity exists in the digestive tract lesions in severe chronic uremia, in which causative factors are more obvious, pathology quite determinate, and undirectional decline inevitable.

Uremia may be defined as a symptom-complex derived from elevation of blood urea, which, in turn, is the result of intrinsic renal disease. On the other hand, azotemia, a more inclusive term, is characterized by an abnormal increase in blood urea, but may result from either renal or extrarenal sources. Significantly, gastrointestinal disorders characterized by vomiting and diarrhea can cause azotemia or retention of urea without the presence of intrinsic renal disease. Typical of involvement in chronic uremia are albuminuric retinitis, fibrinous pericarditis, and ulcerations of the digestive tract.

It has been the lot of all of us in our interne days to treat uremic patients and to note the urinous odor emanating from mouth and nose. More often than not, black, tarry, and frankly blood stained stools contributed a further drain upon their declining blood reserves. The inevitable terminal nature of this complication precluded much further interest in these hemorrhages arising from the digestive tract anywhere from the mouth to the rectum.

The explanation of these ulcerations and hemorrhages has alternated between the toxic and the vascular theories. Historically, Treitz in 1859 propounded the idea that urea was excreted into the digestive tract causing irritation of the mucous membrane by its presence. He was supported by Fischer in 1893, Wurthin in 1932, and Leyrat in 1933. Bereston and Keil in 1941 still adhered to the toxic theory to explain the oral lesions in their cases. The vascular theory, expounding that thrombosis of small vessels in the mucosa preceded the ulcerative phase of these lesions, was promoted in 1898 by Hlava and by Siegmund in 1929.

Two very comprehensive reports have been available on a subject not often detailed in the literature. Data in 1,937 cases from Jaffee and Laing's

thesis reported in 1934, and Mason's 265 cases in an article in 1952, reveal facts that can be neither wholly explained by the toxic or vascular thrombosis theories. Jaffee noted gastrointestinal lesions in 100 per cent of his cases, Mason in only 60 per cent.

Edema of the mucous membrane and hemorrhagic ulcerations were the common findings. Both papers reported about 20 per cent prevalence of ulcerative and necrotic pseudomembraneous lesions. Mason noted that hemorrhage and vascular lesions seemed to underlie the pathological lesions of the digestive tract in uremia.

The toxic theory, emphasizing the caustic action of urea on the digestive mucosa, had been negated because:

1. There was no correlation between the degree of uremia and the necrotic ulcerative lesions;

2. The location of ulceration in the mouth, esophagus and even vagina precluded an urea excretory explanation.

Likewise, vascular thrombosis was not a constant finding. In fact, it was rather infrequent. In contrast, inflammatory vascular lesions were commonly noted, as distinct from the noninflammatory degenerative fibroid arteriolar lesions in the diseased kidney.

Uremia then has hemorrhagic changes through the digestive tract as a rather common finding. Where hemorrhages were most marked, pseudomembraneous and necrotic ulcerations were evident. The necrotic lesions were in those locations e.g. the colon and lower ileum, where bacteria were most prevalent in these severely ill patients with low resistance.

But there still is the problem of what causes these hemorrhages, and it is this field that has been most neglected in research. At the beginning of the twentieth century, Mathieu and Roux suggested that a hemorrhagic tendency existed in uremia. A weakening of capillary permeability or an anticoagulant factor in the blood was postulated; or a combination of the two. A toxin, other than urea, has been suggested. Its effects apparently are obtained through indirect action upon the capillaries, facilitating their rupture, rather than by action upon the intestinal mucosa directly. On the basis of these hemorrhagic lesions, necrosis of surface epithelium occurs. Initially superficial in nature, this destruction gradually becomes deeper. Add infection and necrosis, pseudomembranes are formed. This, in brief, may account for the gastrointestinal bleeding so often seen in these severely ill uremic patients.

FRANK A. MARSHALL

Our Changed Appearance

With this issue, The Review of Gastroenterology departs from its 20 year policy of printing the journal entirely on coated paper.

In our never-ending desire to continually improve, we last year changed the type from which The Review of Gastroenterology was printed to a modern more legible typeface recommended by the Mergenthaler Linotype Co. A continuing survey reveals that the kind of paper on which this issue is printed is more restful to the eye and improves the appearance of the printed page. Illustrations, of course, will continue to be printed on coated paper.

To further enhance the appearance, we commissioned the preparation of a new cover and contents page which also appear for the first time in this issue.

We hope these changes will meet with the approval of our readers whose comments concerning our efforts are always welcome.

NEWS NOTES

Annual Convention of the International Academy of Proctology

All physicians are cordially invited to attend the Fifth Annual Convention of the International Academy of Proctology to be held at the Plaza Hotel, New York City, May 29, 30 and 31st, 1953, directly preceding the American Medical Association Meeting. The meeting this year will be extended to include a Surgical Clinic and Seminar at Jersey City Medical Center under the direction of Dr. Earl J. Halligan. The "Wet Clinic" and Seminar will be on May 28th. An extensive Motion Picture Seminar of Proctologic Surgery (including office technics) will be held on May 31st. All scientific papers will present the latest developments in proctology and gastroenterology.

Because general practitioners, as well as gastroenterologists and proctologists, face proctologic problems in their daily practice, much of the program has been planned to answer their questions.

There is no fee for attendance at the Annual Convention of the International Academy of Proctology. These Conventions, as well as all other activities of the Academy, are directed toward the further development of proctology. All physicians interested in proctology are therefore invited and welcomed to the Annual Meeting.

The program will be available in the near future, upon request to the Executive Offices of the International Academy of Proctology, 43-55 Kissena Blvd., Flushing, N. Y.

Secretary-General to be Honored

Dr. Roy Upham, Secretary-General of the National Gastroenterological Association since 1935, will be signally honored at a dinner to be given by the New York Chapter of the Association.

The dinner will be held at the New York Academy of Medicine in New York City on Monday evening, 11 May 1953, immediately preceding the annual meeting of the chapter.

Dr. Upham's many years of service to the National Gastroenterological Association and to the chapter will be fittingly recognized on this occasion. His many friends and colleagues will attend the banquet.

ABSTRACTS FOR GASTROENTEROLOGISTS

PATHOLOGY AND LABORATORY RESEARCH

A ROENTGEN STUDY OF THE EFFECT OF TOTAL PANCREATECTOMY ON THE STOMACH AND SMALL INTESTINE OF THE DOG: J. F. Weigen, E. P. Pendergrass, I. S. Ravdin, and T. E. Machella. Radiology 59:92, (July), 1952.

Hyperglycemia in depancreatized dogs was found to be associated with delayed gastric emptying and with prolonged small intestinal transit. Hyperglycemia in depancreatized dogs was associated with a normal and, at times, rapid gastric emptying and small intestinal transit time. The absence of external secretion of the pancreas from the intestine did not appear to alter the tone or continuity of the small intestinal pattern or the tone of the colon. Loss of pancreatic function was not shown to alter gastrointestinal motility while the blood sugar was low; its effects could not be evaluated while the blood sugar was elevated.

FRANZ J. LUST

LIVER AND BILIARY TRACT

DIETARY CHOLESTEROL AND ATHEROSCLEROSIS: Esther Tuttle. Geriatrics. 7: 37, (Jan.), 1952.

Insofar as hypercholesterolemia is incident to, or causative of, atherosclerosis accompanying coronary sclerosis, its control requires:

1) a proper dietary approach. Some cholesterol is synthesized in the body. The deprivation of certain fats and other high cholesterol foods is required in a therapeutic diet to lower the blood cholesterol. Exclusion of animal sources of cholesterol and of nonphysiological fats, like hydrogenated fats, diminish the blood cholesterol levels.

2) Oxidation is involved in cholesterol metabolism according to Tuttle, so that drugs like thyroid administered to accelerate aerobic, and particularly anaerobic oxidation, are usually required.

3) Proper Vitamin B formulations are necessary to stimulate enzymatic activity.

4) An outside source of unsaturated fat acids, especially those derived from sunflower seed lecithin or even sunflower seed oil, relieve the liver of desaturation burden and help in the utilization of free cholesterol.

FRANZ J. LUST

THE INCIDENCE OF CHOLELITHIASIS IN LAENNEC'S CIRRHOSIS OF THE LIVER: H. D. Bucalo. Am. J. M. Sc. 224:619-621, (Dec.), 1952.

In order to determine the incidence of cholelithiasis associated with Laennec's cirrhosis of the liver, the necropsy records of 500 cases were studied. No other type of liver disease was considered. The control group consisted of 500 individuals with no liver disease of any kind. This group was controlled for age and sex. Cases of diabetes mellitus were excluded from each group. It was found that 13.6 per cent of the cases with Laennec's cirrhosis had gallstones as compared to 13.2 per cent of the control group. As in the control studies, gallstones occur twice as frequently in women as in men with cirrhosis. The greatest number of cases of cholelithiasis were found in the sixth, seventh, and eighth decades in each group while the peak incidence of cirrhosis

was in the fifth, sixth, and seventh decades. It was concluded therefore, that Laennec's cirrhosis of the liver and cholelithiasis are unrelated diseases, and that the severity of the cirrhosis has no relationship to the formation of gallstones.

J. R. VAN DYNE

THE RELATION OF SERUM IRON TO HEPATOCELLULAR DAMAGE: B. M. Matassarin, N. H. Delp. Am. J. M. Sc. 224:622-627, (Dec.), 1952.

A group of 26 patients with liver disease has been studied by complete liver function profile and serum iron determinations. Serum iron does not correlate directly with any individual test now in use in hepatogram, nor does it correlate directly with bilirubinemia, but it does follow closely the clinical picture. An elevated serum iron level in hepatic disease is evidence of hepatocellular damage as decrease in that level follows recovery. Serum iron determinations have a definite place in hepatographic studies. The elevation of serum iron parallels the extent of hepatocellular damage, provided the blood picture is taken into consideration.

J. R. VAN DYNE

A NEW TECHNIC FOR THE DIAGNOSIS OF CARCINOMA METASTATIC TO THE LIVER: L. A. Stirrett, E. T. Yuhl, and R. L. Libby. Surg. Gynec. & Obst. 96:210-214, (Feb.), 1953.

The authors in this preliminary report use abdominal radioactivity surveys employing radioactive iodine human serum albumin as the tracer material and the scintillation counter as the detector of gamma radiation. Fifty-six patients were studied with this method and the findings were correlated with those of conventional liver function tests and the operative findings. An overall diagnostic accuracy of 96 per cent was obtained in this preliminary series. The test is comparatively simple, rapid, and safe. The method consists of giving each patient a single sterile I.V. injection of 300 microcuries of I-HSA. Twenty-four hours later the patient is placed in a supine position and an anatomical sketch is made of the abdomen over which is placed a guide of coordinate rectilinear points from which counts are made on a scintillation counter. The entire survey can be completed in 30 minutes.

J. R. VAN DYNE

PANCREAS

APPLICATION OF WEST'S TEST IN AFFECTIONS OF THE PANCREAS IN ADULTS: A. Vachon, P. Bonnet, and J. Berthier. Arch. mal. app. digest. 41:29, (Jan.), 1952.

West's test is based on the following principle: the absorption of a solution of gelatine causes a temporary increase in the amount of amino acids in the blood due to digestion of this protein by the trypsin of the pancreas; the curve of amino acidity thus produced is able to give information on the functioning of the exocrine pancreas since gastric pepsin does not produce amino acids and erepsin from the intestine does not attack gelatine.

Applied by West and later by Walgreen in the study of fibrocystic pancreatites in children, this test may also be used with adults when an affection of the pancreas is suspected.

We have used West's test 52 times on 47 subjects of which 29 were check-patients free of any digestive trouble, and 18 suffering from or suspected to be suffering from a disease of the pancreas: 4 cancers, 5 certain cases of pancreatitis, 9 probable or possible cases of pancreatitis.

The basic amino acidity figure varies from 4 to 8 mg. per 100 and the increase, starting from this initial figure, is 1.5 mg. to 2 mg. in ½ hour, 3 to 4 mg. in 1 hour, 4 to 6 mg. (and sometimes more) in 2 to 3 hours; the curve falls afterwards returning to normal after 4 hours or a little later.

A curve is manifestly abnormal when it remains lower than 2 mg. during the entire period of the test, but when at the end of an hour the increase in the amino acid content is not higher than 2.5 mg., the curve may likewise be considered pathological, even if there is a subsidiary rise in the curve.

Out of 4 cases of cancer of the pancreas (two nonicteric cancers of the body and two icteric cancers of the head) the test is positive 3 times and negative once. In two

cases, the curve obtained is comparable to the one obtained by West in fibrocystic pancreatitis in children.

Out of 5 certain cases of chronic pancreatitis in adults, whether or not in association with biliary lithiasis, after an operatory check West's test proved positive in 4 cases: a flat curve below 1.5 in 1 case (diffuse pancreatitis); a curve rising no higher than 2.5 by the end of an hour in 3 cases.

Out of 9 probable cases of pancreatitis, not verified by surgical operation: 5 positive reactions to West's test.

The amino acidity curve induced by the ingestion of gelatine may be applied in pancreatic disorders in adults. It may, if positive, offer a useful complement to the clinical diagnosis and be compared with other laboratory tests. Certain sources of error must be eliminated: in particular, delay in the absorption due to gastric or intestinal stenosis. The test may prove faulty if the excretory canal is not compressed and if lesions allow a sufficient quantity of parenchyma to be secreted.

ACUTE HEMORRHAGIC PANCREATITIS: H. N. Kenwell, and P. B. Wels. Surg. Gynec. & Obst. 96:169-170, (Feb.), 1953.

In 1900 Landsteiner reported the presence of an antitryptic factor in serum albumin. Later studies by many groups have emphasized the importance of antiproteolytic activity in pancreatitis. The author, therefore, animated by a desire to find a substance which might act as an inhibitor to the spontaneous activation of trypsinogen to trypsin in the living tissue, elected to use salt free human serum albumin in the treatment of 11 consecutive cases of hemorrhagic pancreatitis and found impressive clinical evidence that this treatment favorably influenced the course of the disease.

J. R. VAN DYNE

BOOK REVIEWS FOR GASTROENTEROLOGISTS

DISEASES OF THE HEART AND ARTERIES—ANATOMICAL AND FUNCTIONAL DISTURBANCES OF THE CIRCULATION. TREATMENT: George R. Herrmann, M.S., M.D., Ph.D., F.A.C.P., Professor of Medicine, University of Texas, Director of the Cardiovascular Service and Heart Station, University Hospitals, Consultant in Vascular Diseases, United States Marine Hospital, Consultant in Medicine to Surgeon General, United States Army. Fourth edition. 652 pages with 215 text illustrations and 4 color plates. The C. V. Mosby Company, St. Louis, Mo., 1952. Price $12.50

The author of this excellent volume in the new fourth edition, has brought the work uptodate. Professor Herrmann has been a close student for many years of this particular subject and has taught many physicians and medical students over the past two or three decades. He is well read in the field of cardiology and has kept abreast of recent advances, and of the rapidly increasing literature on diseases of the heart and arteries. This practical work contains much of what is new and helpful to the student and the practitioner, to the clinician, specialist and teacher. All the important phases of our knowledge of diseases of the heart and arteries are satisfactorily and adequately considered.

This work is highly recommended as one of the best, practical and informative books on the subject now available for use of medical students, practitioners and clinicians. Such topics as ballistocardiography, vectorcardiography, electrokymography, angiocardiography, cardiospectrograms, sound recordings, etc., will no doubt receive consideration by the author in a future edition.

TEXTBOOK OF CLINICAL PARASITOLOGY: David L. Belding, M.D., Professor of Bacteriology and Experimental Pathology, Emeritus, Boston University School of Medicine. Second edition. 1139 pages. Appleton-Century-Crofts Inc., New York, N. Y., 1952. Price $12.00.

This much improved second edition of an excellent one volume work on clinical parasitology by an experienced teacher and expert parasitologist is a most useful and satisfactory volume for students, physicians, public health officials, biologists, laboratory workers and Army, Navy and Air Force personnel of the various medical divisions.

The first edition appeared ten years ago. Experiences of the two great wars and our Marshall Plan (medical and public health) assistance, now world-wide in extent, make such a volume of great value at this time.

This volume is gladly recommended by the reviewer as the latest work on parasitology with such understandable and readable consideration, including useful tables and graphic representations.

THE 1951 YEARBOOK OF PATHOLOGY AND CLINICAL PATHOLOGY: Edited by Howard T. Karsner, M.D. and Arthur H. Sanford, M.D. 454 pages, illustrated with an author's name index and an elaborate cross index. The Year Book Publishers Inc., Chicago, Ill., 1951. Price $5.00.

The section on general pathology includes a comprehensive index of subjects including epidemic hemorrhagic fever. This is a special article well documented and enlightening. The infective organism has not been identified and therefore, a soldier returning from Korea to the United States may become ill with fever, nausea, vomiting, thrombocytopenia and mild leukopenia, subconjunctival congestion, hematemesis, etc., should be carefully studied to rule out the above infection.

Enos and Elton call attention to Chagas' disease in the Canal Zone. On pages 157-58, cat scratch disease is discussed. Beginning with page 180, the alimentary tract and associated glands are discussed. On page 271, Boles, Sr. and Boles, Jr. describe Wernick's disease and its probable etiology. Thiamine and other B-Complex Vitamins are advocated in the therapy. The editor of this section of the volume disagrees with the possible usefulness of the vitamins when the case is well advanced.

The second part of the book deals with laboratory procedures and newer methods in laboratory technic, apparatus, etc.

THE 1951 YEARBOOK OF ENDOCRINOLOGY: Edited by Gilbert S. Gordan, M.D. 415 pages, illustrated, including tables. The Year Book Publishers Inc., Chicago, Ill., 1951. Price $5.00.

Beginning with the pituitary gland on page 8, the volume ends with miscellaneous studies, such as endocrine studies in aging, hormone excretions in patients with chronic liver disease, studies in disorders of muscle in progressive muscular dystrophy, an endocrine or metabolic disorder, etiology and treatment of serum potassium deficits and potassium replacement solutions and much other instructive and informative material which the physician would miss unless he has the time and inclination to read the many American and foreign medical journals.

The 1951 Yearbook of Endocrinology is recommended to all physicians who are interested in following the progress of research and recent development in endocrinology.

THE 1952 YEARBOOK OF MEDICINE: Edited by Drs. Beeson, Amberson, Castle, Harrison, Esterman and Williams. 735 pages, profusely illustrated in black and white, line drawings and tables. The Year Book Publishers Inc., Chicago, Ill., 1952. Price $6.00.

As year after year "The Yearbook of Medicine" appears under the editorship of the well-known clinicians, the physician will find a wealth of new and instructive material culled from the medical literature.

The sections on infection, the chest, the blood and blood forming organs, the heart and blood vessels and the kidney, the digestive system and metabolism are replete with diagnosis and therapeutic suggestions with comments of the respective editors.

The name and subject index enhance the value of this volume as a ready reference.

PHYSICAL DIAGNOSIS: Harry Walker, M.D., F.A.C.P., Professor of Clinical Medicine, Medical College of Virginia. 161 pages with 126 illustrations. The C. V. Mosby Company, St. Louis, Mo., 1952. Price $8.00.

The thirty-eight chapters of this new work on physical diagnosis cover the usual subjects, such as recording the physical examination, speech, gait, station, habitus or build, body temperature, inspection of the head, forehead and ears, of the mouth and throat and of the neck, upper extremities, thorax, etc. Diseases of trachea, bronchi, lungs, pleura, diaphragm, circulatory system and the abdomen are all briefly discussed.

This work should be helpful to medical students and nurses as a systematic outline and guide in physical diagnosis.

PROGRESS IN NEUROLOGY AND PSYCHIATRY—AN ANNUAL REVIEW, VOLUME VII: Edited by E. A. Spiegel, M.D., Professor and Head of the Department of Experimental Neurology, Temple University School of Medicine, Philadelphia, Pa. 604 pages. Grune and Stratton, New York, N. Y., 1952. Price $10.00.

The editor and his many excellent contributors have informatively and carefully reviewed the literature and satisfactorily presented basic sciences – neuroanatomy, neuropathology, neurophysiology, pharmacology, neurology, neurosurgery and psychiatry.

This volume is recommended as a helpful and very instructive review of the exhaustive literature on these subjects. Neurologists, psychiatrists, clinicians and general practitioners interested in these topics can use this work for a time-saving review of the recent literature.

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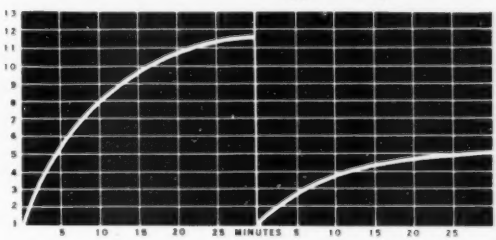
1. Smith, F. H.: *Gastroenterology*, 8:494, Apr., 1947.
2. Woldman, E. E.: *Am. Jour. Med. Sc.*, 194:333, Sept., 1937.
3. Fox, J. R.: *Jour. Lancet*, 72:361, Aug., 1952.

In hyperacidity



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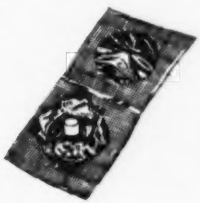

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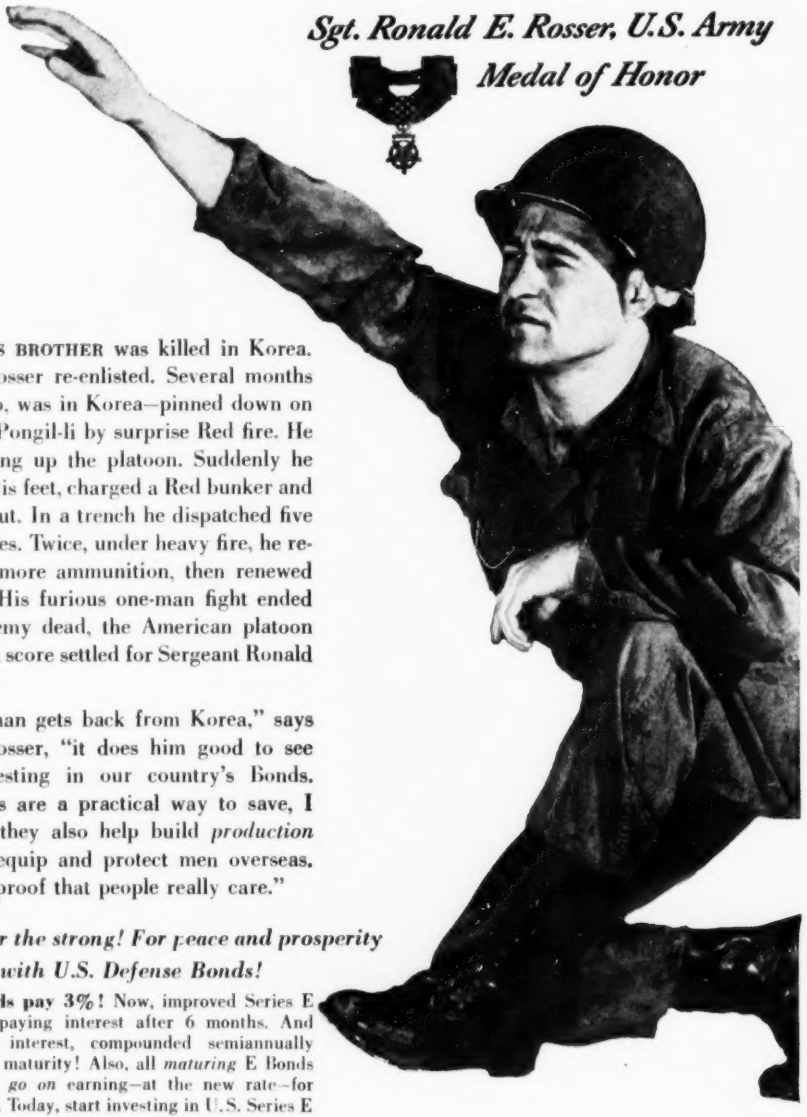

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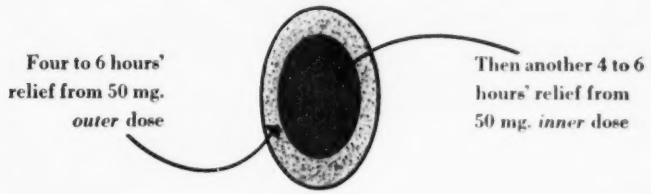

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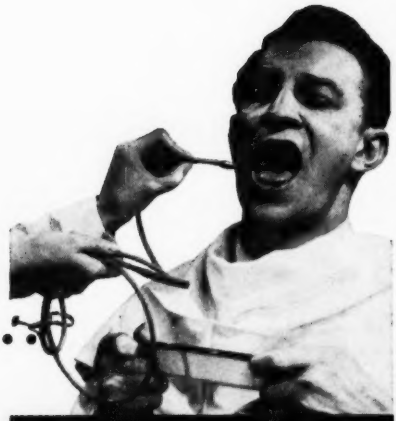

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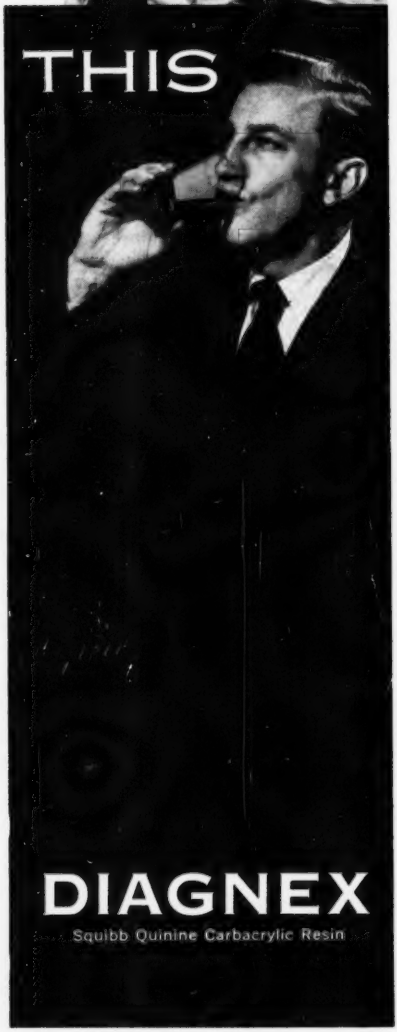

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